Vasculitis

def. Specific pattern of inflammation of the BVs wall That Can affect any body system & has clinical finding ranging from: Erythema & urticaria to purpura, Necrosis, & ulceration

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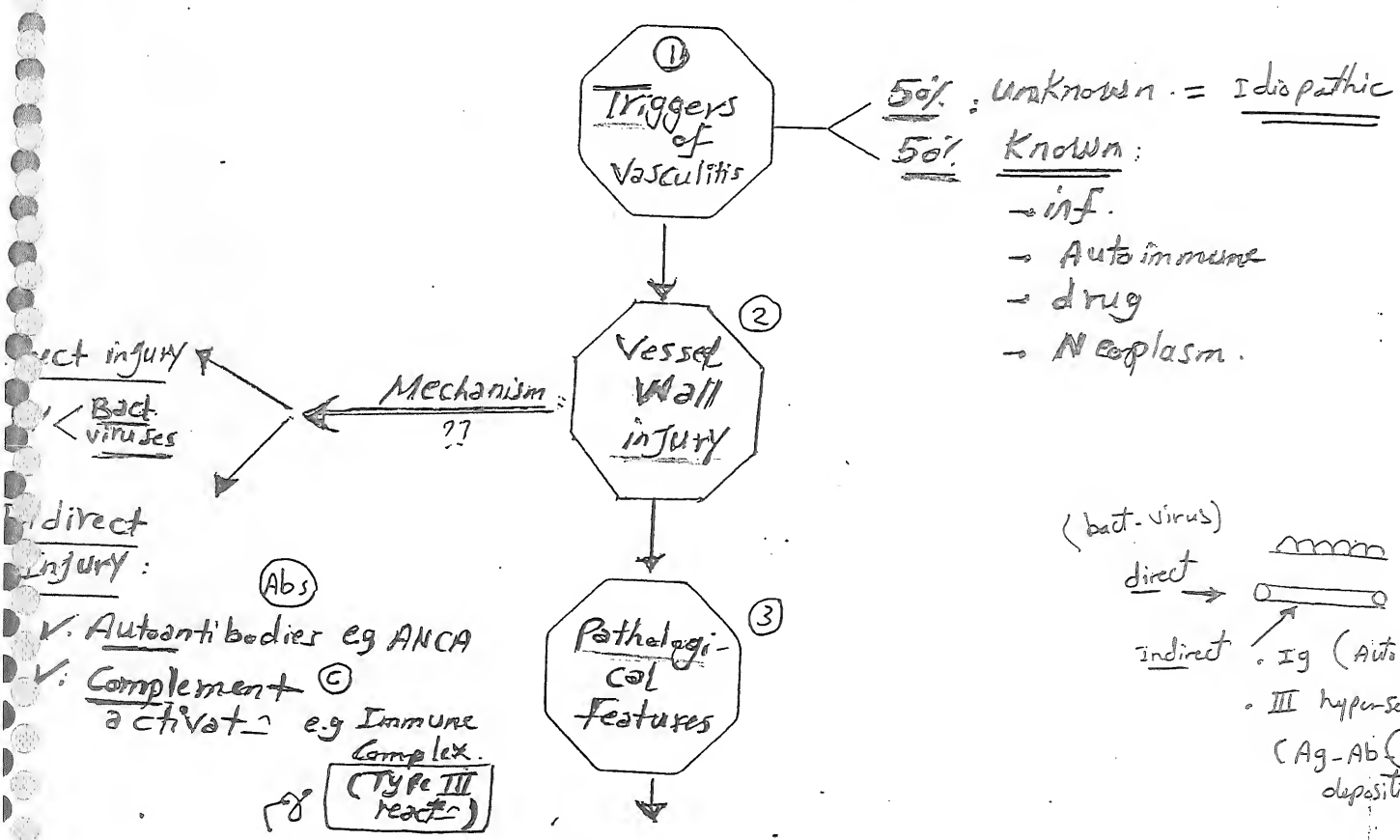
Pathogenesis of Vasculitis



Pathological features of (HIP) Vasculitis. (Triad). Δ

H/p * Vasculitis :-

(2)

△ ① Fibrinoid Necrosis ⊂ Endothelial swelling + Fibrin deposit ⊃ (Eosinophilic strands) in & around Vs Wall

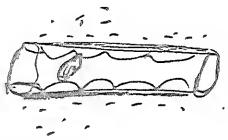
Wall

→ Smudgy appearance

o/s ② Perivascular Infilt ≤ inhlt inflamm destruction of bl. vs wall

③ Less essential features :-

- Edema
- RBCs extravasation
- Vs Wall infilt.
- Luminal thrombus.
- Leukocytoclasia ✓



* Vasculopathy = pseudo vasculitis :-

- Fibrinoid deposit ↑ ē (No) inflammation
- Vs Wall infilt ē ± (No) alterat⊃ ← minimal.
- Leukocytoclasis "ē out" fibrinoid degen.

(NB)

Type (I) hypersensitivity → urticaria

(II) → drugs

(III) → vasculitis

(IV) → CMI (as) Contact dermatitis (CD)

Serious drug :-

- Allopurinol
- Septrine
- Anti Convalsant.

Histopathological features are essential for ∅ of Vasculitis (3 Cs)

1. Fibrinoid degen. (or) Necrosis: endothelial inflamm + Fibrin deposits in & around / Vs Wall → Eosinophilic strands (E) smudgy appearance of BVs.
2. Angio centric (Perivascular) (or) Angio invasive (Vascular Wall) infiltrates.
3. Vs Wall disrupts (or) destructs

NB: Non essential features → Edema, Ulcerats, RBCs extrav.

Q: الفرق بين Vasculitis & Vasculopathy

Vasculopathy: Fibrin deposits, Thrombosis, Vs Wall infiltration without disrupts or destructs (No inflamm) (No fibrinoid degeneration)

Classificats of Vasculitis: (No universally Accepted Classificats):

- Cute: < 4wks — purpura, Ulcerats, Systemic manif..
- hr: (mild) > 4wks — macules, papules. No systemic manif.

Classificats may be According to:-

1. Size of involved Vs. (Small, Medium, Large)
2. Type of infilt.
3. onset: Acute, & chronic.
4. Etiology: 1ry (Idiopathic) or 2ry → Inf., Autimmune, Drugs, Mg.
5. Extent: Cut. (localized) or Systemic
   - Cut. affects only
   - Systemic → Systemic organ affects

Most Common 3 organs:-

- GIT: NV, abd. pain & (Melena)
- Joint: Arthralgia & Myalgia.
- Renal: HTN, Hematuria & Edema

Others:
- CNS: Parasthesia
- CVS: Chest pain & CHF
- RT: dyspnea & Cough
- General: FAHM

According to infilt

(4)

⊡ Lymphocytic

- AICTDs
- EM
- Behcet & PG
- pLEVA
- LYP
- GVHD
- Angiodestructive ← Lymphoma / Lymphoma-Granulomatous

⊡ Eosinophilic

- Granuloma facial
- Hyper-Eosinophilic Synd.
- Churg Strauss
- ± AICTDs

⊡ Granulomatous

- Takayasu
- Giant Cell
- Nodular Vas
- Wegeners
- Churg-Strauss

← Es.
← granula
← IGD

⊡ Incidental

- Sweet
- PG

1- Immune Complex Vs

1- predominant IgA ← idiopathic HSP / drug / infection
2- ~ IgG, IgM → idiopathic, drug, infect
3- Mixed cryoglobulinemia
4- Rheumatic Vs asse AICTDs

2- PNG Immune Vs

- ANCA ← MPA, WG, CSS
- EED
- GF
- Sweet
- Cut PAN
- some pustular Vs

(NB) **Localized Types of Vasculitis**

- EED
- GF

5- some pustular Vs
6- Bn hypergammaglobulinemic purpura of Waldenstrom.

CHCC 2012 Classification (Acc. to size of BV) (5)

Aorta

1- Large Vs Vasculitis: (Aorta).

- Giant Cell arteritis
- Takayau's arteritis.

deep dermis

(50-150μ) 2. Medium Vs. Vasculitis: (Cut. aa: in deep dermis & S.C.T, Coronary, hepatic) & Renal

- PAN
- [KD] → - Kawasaki's dis. (Coronary not cut Vasculitis) ×

upper dermis

(<50 μ) 3 Small Vs Vasculitis: (arterioles, Capillaries, post Capillary Venules in upper dermis)

↓

2 Types

- **ANCA associated**
  - Wegener's Granulomatosis (WG)
  - Churg - Strauss (CSS) Synd.
  - Microscopic Polyangitis (MPA)
  - Drug induced. - Idiopathic
- **Non ANCA Associated**
  - LCV
  - urticarial Vasculitis (UV)
  - ? HSP
  - EED
  - Cryoglobulinemia.
  - AHEI

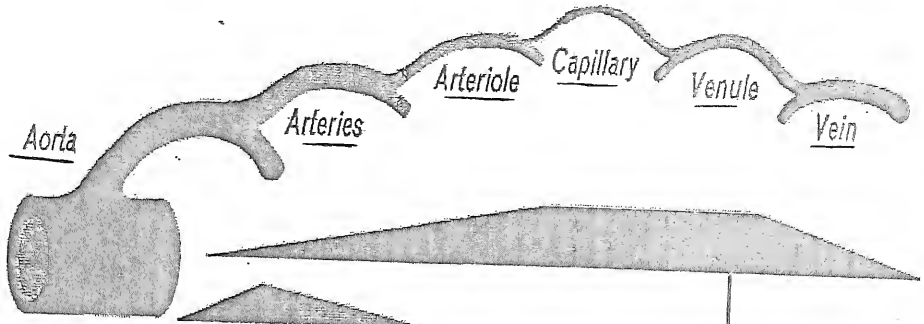
  (& infant)
  - ENL

4 Variable Vs Vasculitis
- Behcet
- Cogan Synd.

5 Vasculitis With Systemic dis:
- Lupus Vasculitis
- Rheumatoid "
- Sarcoid "

6 Vasculitis ass. & Probable Etiology
- HCV ass. Cryoglob. / HBV ass, Drug

Small-med. sized
- Cryoglob.
- ANCA Vasculitis



- **Large vessel vasculitis**
  - Granulomatous arteritis in a patient >50 y → **Giant cell arteritis**
  - Granulomatous arteritis in a patient <50 y → **Takayasu arteritis**
- **Medium vessel vasculitis**
  - Necrotizing arteritis without MCLN syndrome → **Polyarteritis nodosa**
  - Necrotizing arteritis with MCLN syndrome → **Kawasaki disease**
- **Small vessel vasculitis**
  - Immune complexes in vessels
    - Other sources for immune complexes → **Other Im Cx vasculitis**
    - Cryoglobulins in blood and vessels → **Cryoglobulin vasculitis** → HCV
    - IgA dominant vessel wall deposits → **H-S purpura**
    - SLE or rheumatoid arthritis → **SLE/rheumatoid vasculitis**
  - Paucity of vascular Ig (often with ANCA) — ASSE + ANCA
    - 0 Vasculitis with no asthma or granulomas → **Microscopic polyangiitis** (MPA)
    - 1 Granulomas and no asthma → **Wegener's granulomatosis** (WG)
    - 3 Eosinophilia, asthma, and granulomas → **Churg-Strauss syndrome** (CSS)

Small Vs Vasculitis

(7)

1 - Leukocytoclastic Vasculitis (LCV)

(Cut. SVV [CSVV] // Allergic or Hypersensitivity Vasculitis)

Def Small Vs Vasculitis that's ch BY:

- clinically: painful palpable purpura (3P)
- pathologically: Leukocytoclasis (+/-2) → angiocentric / Angio Invasive infilt. Vs wall destruct. ± fibrinoid degen.

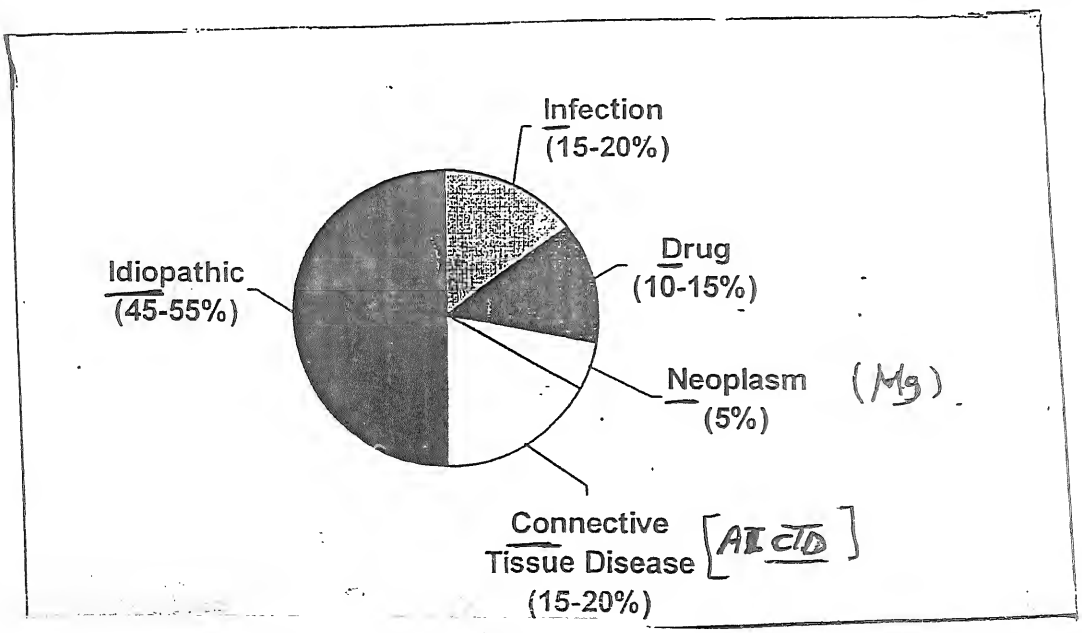
pathophysiology: Triggers → Immune Complex deposit. (Type III react.) → pathological changes of Vasculitis

((Ag-Ab))

Etiology:

Triggers

- 5% Idiopathic → Called "1ry Vasculitis"
- 50% Known causes → See below → Called "2ry Vasculitis" ← infect, Mg, drugs, AI CTDs



• Known Causes of Vasculitis:

(8)

A. Inf: (15-20%)

1. Bacterial:

- Staph. (rare)
- Strept
- E. Coli
- Brucella
- Salmonella
- Mycobact.
- Chlamydia.

2. Viral:

- HCV > HBV > HAV (Also their Vaccines)
- HIV
- VZV (rare).

B. Autoimmune C.T dis: (15-20%)

also "IBD"

- SLE
- Sjogren → SS
- RA → Autoantibodies → Vasculitis
- DM

C. Drugs: (10-15%)

أي دوا ممكن يعمل ولكن أشهرهم:

- Antibiotics (Beta lactam) (also • Minocycline • Quinolones)
- NSAIDs.
- ⊙ Thiazide diuretics
- ⊙ Thiouracil
- • Anti Coagulants (Warfarin & Coumarin)
- • Anti thyroids
- • Anti TNF.

D. Neoplasm (2-5%)

- Leukemia
- Lymphoma
- MM
- Carcinomas.

E. others: (3F)

1. Genetics:
   - FME
   - Immunodef. Synd
2. Food & its Additives (Tartrazine)

CIP

LCV

± Cut ± Systemic

1- Cut. manifs. of LCV:

- Bilat.
- Symmetrical

LL = • site → at dependent sites & sites under Tight "Tight Clothes" (ملابس ضيقة)

• Symptoms: Asymptomatic but ± pain, Burning or Itching

• Lesion:

Typically

3P: Painful, Papable (±) ulcer, Purpura

Less Common

- Urticarial like (more in chr. cases)
- Nodules
- Livedo Reticularis. (LR)
- Retiform purpura. (Rp)

2- Systemic manifs. of LCV: (جدول بولونيا)

اسأل عن الأعراض

(i). Commonest 3 organs affected:-

- GIT → AN - AP - Melena
- Joint → Arthritis - Arthralgia
- Renal → Haematuria - Eodema - HTN.

(ii). Other organs: CNS, CVS, RT, General.

- CNS → paresthesia
- CVS → dyspnea, chest pain
- RT → Cough
- General → FAHM

Course (prognosis) of LCV:-

(90٪) ← 1. Acute LCV = ch. By:

- Severe Cut. affect = (purpura & ulcerat=)
- Mild systemic "

ومش دايما resolut= ē in 4 ws (3-6 ws) [90٪]

(10٪) ← 2- Chr. (Re current):

- Mild Cut. affect = (macules, papules & urticaria)
- X · (No) systemic "
- Remission & Exacerbat= for > 4 ws. (at) ms-ys intervals.

LCV has good prognosis

So prognosis of LCV is good ē 90٪ of cases show spontaneous resolut= within 4 ws while 10٪ will have recurrent (or) chronic dis.

predictors of chronicity:
- Arthralgia
- Cryoglob.
- No fever

Evaluation of A Case of LCV (Diagnosis)

عايزين نعمل ٣ خطوات

1- Confirm the clinical diagnosis by Histopathology & DIF. . - < HP DIF

2- detect systemic involvement — Syst affect

3- detect the Etiology (in 20٪ cases). — AET

1- Confirm the clinical Dx by Histopath. & DIF:-

لازم العينة تتأخذ بين ١٢-٢٤ 12-24h

path → Leukocytoclasia? + Vasculitis (≥ 2 criteria)

precautions:- ± others.

- Too early (<12 hr) or too late (>24 hrs) → may be -ve → Biopsy
- after >24 hrs → -ve (IF)
- Eosinophils → indicate drug Etiology.

Leukocytoclasia: Neutrophilic degranulation & fragmentation & nuclear dust formation in Dermis (Nuclear karyorrhexis)

DIF: granular deposits of C_3, IgG, IgM, IgA at Vs. Wall.

2 Detection of systemic affection: BY:

Hx • History
Clp • Clinical Exam.
Inv • Invst e.g CT, XR, Urine, CBC, ...

3 Detection of Etiology of Vasculitis: (in 2ry Type)

(a) Hx of: - Drug
- inf.
- Food Allergy
- Ass. systemic dis. (AICTDs)

(b) Lab:
- CBC, ESR, ASO → - CRP, ↓ FT, < RFT
- → ANA
- ANCA
- ← Cryoglobulins
- Complement level (ph) ← (SLE / UV)
- Urine analysis.

(c) Rad.: CT scanning for possible Mg ← Cause

Treatment of LCV

(Should it be aggressive as Majority (90%) of cases are self limiting without systemic manifs.)

(١٩٠) هتخف لوحدها من غلاف عجوز

- Cut. affect⁻ only.
  - Mild cut. (No ulcerat⁻)
    - Supportive Care
      - Antihistamines
      - NSAIDs
    - ⊙ Pentoxiphylline
    - Dapsone
    - Colchicine.
    - ⊙ Trental
  - Severe Cut. (ulcerat⁻) ← أتفضه
    - v. Thalidomide.
    - v. MTX (low dose Weekly)
    - v. prednisone. (Cs)
- systemic affect⁻
  - Cs
  - (AZathiop. / Cyclosporine / Mycophenolate -M.)
  - IFN-
  - IVIG
  - ECP
  - Infleximabe

ابعته باطنه كان

Immuno-Sup 3rd li

⊙ Supportive Care :-

1- Rest راحة
2- Leg Elevat⁻ ترفع رجل وتريحل
3- Avoid Trauma & Cold بلاش تخبيط
4- remove The offending Ag

تحويل عيادات :-

- ⊙ باطنة
- ⊙ كلى
- ⊙ روماتيزم → AI CTDs = e.g RA DM
- ⊙ صدرية
- ⊙ عصبية

2- Urticarial Vasculitis (UV): (Leukocytoclastic Vasculitis)

- Def: recurrent Episodes of [painful, persistent (>24hr)] [urticarial-like lesions] with or without Angioedema (±) (frequent)
- Incid: unknown but (≃ 5-10%) of cases having ordinary urticarial wheals shows UV on pathology.

Female > 30-50y

أعمل [circle test] ← Wheal دايرة عليه وبعدين شوف هيختفي امتى

- Etiology ① Idiopathic (most)
  ② 2ry to:-
  - Inf. (sp. HBV, HCV & [EBV])
  - Autoimmune (sp. SLE & SS)
  - Drugs (sp. [KI] fluoxetine & NSAIDs)
  - Neoplasms.

- C/P: urticarial Vasculitis is [very similar] to Wheals of ordinary urticaria but [differs] in:-

1- lesions lasting >24 hrs. (persistant)
2- (Painful) rather than pruritic. (Burning or)
3- on healing → Postinflamm. Hyperpigm. (PIH)
4 [Path] → as LCV.
5 with [diascopy] → Hge (sometimes subtle) can be observed.

However other features don't always present. 5-10% of ordinary urtic. → UV By Hx

⊙ Types of Urticarial Vasculitis:-

(14)

Normocomplementemic (Most cases 70-80%)

⊙ Ch By:
- Mild.
- self limiting
- affect skin only (No systemic)

⊙ NL Complement level.

↓

Mild therapy

Hypocomplementemic (less common) (HW)

⊙ Severe
- Cut-& Systemic affection.

⊙ Hypocomplementemia:-
- ↓ C1, C3, C4
- (+Ve) Anti C1q antibodies.

→ • (±) Ass. with:-
1. AICTDs: SLE, SS, RA
2. HCV, HBV
3. Serum Sickness
4. Schnitzler Synd.

→ • System manifs:-
- ⊙ Angioedema
- ⊙ COPD
- ⊙ Arthritis
- ⊙ Uveitis
- ⊙ GN.

Arthralgia
Abd pain
Uveitis
low grade fever
GN

NB: ↘ aggressive therapy

→ • Schnitzler's Synd.:
- UV + Monoclonal IgM gammopathy + ≥2 of the following:
  - Fever
  - LN
  - Arthritis
  - boneache
  - HSM
  - ↑ESR
  - ↑ WBCs

UV
↳ IgM gammopathy
+ (2) NL

Fever, LN, HSM
↑ESR, ↑ WBCs
Arthritis, Boneache

3. Henoch-Schonlein Purpura (HSP)

IgA

(Anaphylactoid purpura)

- **Def.** Type of (SVV) That Typically affects children (<10Ys) following (R.T) inf.

- **incid.**
  - ⊙ Commonest Type of Vasculitis affecting children.
  - ⊙ **Age**: Typically [4-8Ys] but adults may be affected. · **Sex**: [Boys > Girls.
  - ⊙ **Season**: More in [Winter]

- **Pathogenesis**: → Immune Complex deposit⁻ (IgA) DIF IgA + C3 Fib.

- **CIP**: Boy (4-8Ys) ⟶ URTI (strept / viral) ⟶ 2 Ws →

Tetrad of: P A P A H

(100%) (Purpura) (P)
- at Lower extremities & buttocks. (النمط الخافق)
- resolve ē in [6-16 Ws] but recurrence ± occur (5-10%)

(Abdominal Pain) (90%)
- Simulating Acute abd.
- Paralytic ileus & intussucept⁻ may occur.

(Arthralgia) & Arthritis (60%)
- ⊙ of ankle,
- ⊙ Knee
- ⊙ L.L Edema

Scrotal Edema (2-3%) → Doppler to DD Torsion

(Hematuria) (40%)
(Renal involvement) ↓ (4%)
- usually mild (Mic. Hematuria & minimal proteinuria)
- SDF limiting ← ⊙ only: (2%) will → (RF) (2%) show renal impairment (Hafold risk > N.S)

Renal affect⁻ may occurs after appearance of Rash by ≃ [3 ms] ← علشان كده متابعة البول لضغط الدم ٣ شهور

⊙ **Renal affect⁻ in (Adults) more Common** أعلى **specially if:** لو
1. Fever
2. ESR
3. Rash above the waist. [فوق الوسط]

Poor prognostic factor:-

1- RF at time of onset
2- Nephrotic synd
3- HTN
4- ↓ Factor XIII activity

HSP

1-ACR: ≥ 2 Criteria	2- European League Against Rheumatism (EULAR), 2006
ACR 1990 1- Palpable purpura (3P) 2- onset ≤ 20y 3- Abd pain 4- H/p: granulocyte in small bl.vs	TABLE 1. European League Against Rheumatism and Paediatric Rheumatology European Society Criteria for Vasculitis ★ Mandatory criteria ✓ Palpable purpura (3P) 1 ★ Plus at least one of the following criteria: + Diffuse abdominal pain 1 + Immunoglobulin A deposition in any biopsy (IgA) → in Biops. Arthritis/arthralgias Renal involvement (hematuria and/or proteinuria) Adapted from [illegible]

PAPAH + (IgA)

IgA vasculities:-

- HSp
- Mixed cryoglobulinemia
- Rh vs
- Livedoid vs

- Pathology & DIF: (↑ preserved Morphology. الأنسجة سليمة)

LCV ← + Leukocytoclasia
dermis [(Nuclear dust) (Neutrophilic degranulation / fragmentation)

"predominance of "IgA" + C_3 (في الأوعية) within bl.vs wall
also C_3 fibrin

- Invs: → (علشان الفحوصات ..)

1- ESR سرعة ترسيب ✓

2- تحليل بول وبراز
urine / stool for < Mac. & MiC. (لو معاه) Hematuria & Proteinuria.

3- ضغط الدم ← لو زاد ← لفترة (٣ شهور)

US → (لو فيه التهاب بيتحصل (Ileocolic) ← Bp

Biopsy ← P AP A H
- ESR
- Urine, BUN
- Bp
(٣ شهور)
- Barium enema
- US
- Stool

4- أشعة بالصبغة على الأمعاء
Barium enema / US
"Spiking (or) Cobble stone appearance of intestine"

5- Skin Biopsy = عينة جلد ✓

Criteria of D:-
1. ACR الجدول
2. EHCC Criteria:
LCV + IgA ← deposits.

(٤ معايير) 1+1 (3 من ٥)

Treatment
(mainly supportive)

P (purpura)
- Dapsone
- Colchicine

AP (Abd. pain)
- NSAIDs.
- H_2 Blockers.
- Cs (Effective > analgesics)

A (Arthralgia)

H
- Hematuria & Nephritis
- Use of (Cs) or other Immune Suppressives in HH (or) prevention is Controversy

also **IVIG** indicated if:
- resistant purpura
- persistent Abd. pain.
- → arrest Progressive GN.

4- Acute Hemorrhagic Edema of Infancy (AHEI)

(Finkelstein's dis = Infantile postinfectious Iris like Purpura & Edema)

Edema FAHM ~5, Targetoid purpura ← AB's & URTI عند عيال سنين ← تجمع خلال ٤ أسابيع

Ch BY

* Age < 2Ys (4 ms - 24 ms)

* Recent history of:

HX
- URTI (staph, strept, Adeno) أو فيروسي
- Antibiotics

* Lesions: Abrupt onset of Cockade, annular or Targetoid purpuric lesions involving:

Acral
- Face
- Ears
- Extremities

Then spreads proximally To involve scrotum & Trunk

* Ass. with: Scrotal / Acral Edema & (+) FAHM.

Torsion لازم نفرق

ملخص

- <2Ys, URTI or Antibiotics → Abrupt & annular & Targetoid purpuric lesions; firstly Acral → Proximally ass. c Acral Scrotal Edema & FAHM 1-3 ws → Spont. Resolution

خلاص

* Fate → Spontaneous recovery within 1-3 Ws. Without Sequele.

DD
- HSP
  - EM
  - Kawasaki
  - Meningococcemia

Similarity
- following URTI
- favors ♂
- seasonal (شتاء)

X but AHEI differs in:
- Younger Age (<2y)
- Resolve quickly
- Lacks IgA on DIF
- Rarely ass. c systemic Sympt.

* Tt
- 1st line → supportive
- 2nd " → anti Histamines
- 3rd " → Cs

Gottron papule of RA

diurnal variation

5- Erythema Elevatum Diutinum (EED)

(Chr- fibrosing LCV). (updated 2012).

C/P → Multiple, Bilat, Symmetrical
- Papules,
- Nodules & Chr By:-
- Plaque
- ± ulcers & Blisters

Etiopathog (Triggers)
- Inf: Bact: Strept / Viral: HBV, HIV
- Hematological Mg: (BCL) MM
- Rheumatological dis
- Ig A Gammopathy (SLE)
- GF

IL 8 plays a role

① - Violaceous, red-brown or Yellowish

② - Early: (Soft), Later → (Hard) → fibrosis

③ - Site: over joints of Hands, feet, Knees, Elbows, palmar Eminences, buttocks, Tendon Achillis (Pressure Areas)
(✗ → (Sparing the Trunk) ✗✗

- Age: 30- 60 yrs
  - ♂ older (Hutchinson Type)
  - ♀ younger (Bury Type)

④ - May show Central Clearance & diurnal Variation (يزيد نهاراً وقل ليلاً)

⑤ - Common Ass. ≥ ocular affect → اتابعل

⑥ - Very chr. & persistent: resolve ≥ in 5-10 Ys (but may last upto 40 Ys)

⑦ ± → Atrophic scars.

- Pathology ① Early cases: → LCV (DIF ← C, IgG, IgA, IgM) البت عن

② Late Cases (Zosis)
- Extracellular Cholesterosis (EC) (Lipid & extracell. cholest deposits) → Yellow (لونه عشان كده)
- + Fibrosis (onion like perivascular) → hard (عشان كده)

(لاستخدم لانها ممكن تعمل)

- Treatment:
  - Dapsone (لازم) (For: Long Time)
  - IL Cs (systemic not indicated)
  - Nicotinamide
  - PLEX: intermittent plasma exchange (Severe Cases) (بيت →)
  - + Sulphapyridine

6- Cryoglobulinemia.

Def: presence of abnormal Immunoglobulins that precipitate at cold Temperature & redissolve on rewarming (at 37°C) e.g (presence of abnormal Cold Precipitable Igs)

vasculopathy → (IgG + IgM + C)

Vasculitis → (Ig)

Types of Cryoglobulinemia: (Brouet classification):-

Type & %	Ig Type	Immune Complex	Associations
Type I (10%)	Single Monoclonal IgM (less common IgG)	X None Vs occlusion	↙ Lymphoproliferative disorders: • Leukemia • Lymphoma • MM • Macroglobulinemia (Waldenstrom's)
Type II (60%) (mixed Type)	Monoclonal / polyclonal (Monoclonal IgM ē +ve RF* against Polyclonal IgG)	Vs IgM-IgG (+ IgG-IgG or IgA-IgG)	HCV - AICTDs - lymphoproliferative HCV (90%) CTDs: ↙ RA (45%) • SLE (25%) • SS (Sjogren) (15%) • Systemic sclerosis (10%) (SSc) ⊙ others: HBV (5%) HIV (25%) ← Lymphoproliferative (5%)
Type III (mixed Type) (30%)	Polyclonal / polyclonal (Polyclonal IgM ē +ve RF against Polyclonal IgG)	IgM-IgG (+ IgG-IgG-IgA)	

Clinical: Raynaud's Phenomenon, Retiform purpura, gangrene, acrocyanosis, palpable purpura, PN, arthralgia, GN

[B] RF: Rheumatoid factor activity = means that this IgM can bind to (Fc) portion of IgG.

HCV: is the most common cause of cryogl.

NB - Type II & III are

- Commonest types.
→ called "Mixed Cryoglobulinemia" or "Cryoglobulinemic Vasculitis" because they cause Vasculitis but Type I don't cause Vasculitis [but Vasculopathy]

Another old classification
Type Essential (idiopathic)
(Y (d.t underlying Et.)

- Pathophysiology of Vascular damage in Cryoglob. :-

• Type I (No Immune complexes): → Vascular occlusion (d.t ppt & thrombosis) = (Vasculopathy)

NB
- Median age: 60 y
- Cryoglobulins are +Ve in low titre in 50%

• Type II & III (+ve Immune Complexes): → Vasculitis (LCV).

CIP of Cryoglobulinemia

1- Type I (only Cut manifs, No Systemic affect but ± renal):

Mostly Acral
- Retiform purpura
- Acrocyanosis
- Raynaud's

→ Peripheral Vascular insuff → occlusion vs

- Arterial Thrombosis
- Gangrene.
- Cold urticaria.

2. Type II & III: (Cut & Systemic) :

- 3P (but ± urticaria, Livedo, retiform purpura, leg ulcers)
- Arthralgias 70%.
- PN (sensory ++ & motor weakness).
- GIT dis & Hepatitis.
- G.N.

Tetrad: PN. purpura. arthralgia. Renal dis

skin
GIT
Joint
GN
PN.

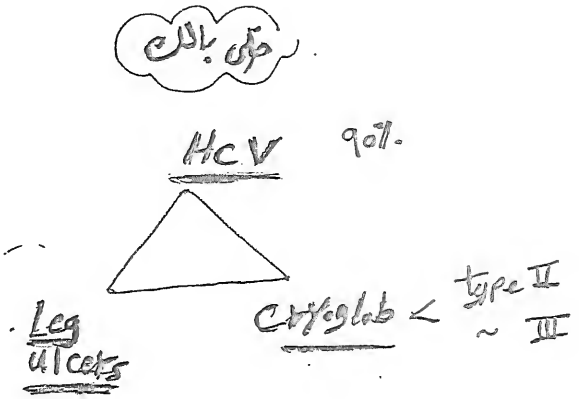
(Ulcer & purpura) around Ankel

↓

Mixed Cryoglobul

↓

HCV



- Type I → Mg = (lympho proliferative dse)
- Type II & III → Infection & Autoimmune [AICTDs, HCV]
  - IgM → RH
  - → DD
    - [Cryoglob.
      - PG
    - [Artefacta = (dermatitis artefacta)
      - Ecthyma Gang.
    - [Calciphylaxis.
      - Necrotizing fasciitis.

Invs: ① Tests for Cryo-globulins :-

لو طلعت سلبية نفيدها كذا مع اثناء ال ((Clinical attack))

يجب عينة الدم في أنبوبة عند درجة حرارة ٣٧°.

تترك لتجلط ثم تفصل الـ Serum عن الـ Centrifugate بالطرد المركزي.

تحضن عند درجة Incubator لفترة: (4°C) لمدة 24h لـ Type I و 7 ds لـ Type II

Blood sample 37 → Serum Centrifuga → Incubator 4°C (ppt)

Serum → Centrifugate

Tt of Cryoglobulinemia :-

Underlying AE

- e.g HCV 90% (IFN-α, Ribav.)
- CS (Cyclosporine)
- Rituximab / IVIG

- Type I → ppt within 1st 24 hrs (at conc > 5mg/ml)
- Type II → ppt at ≈ 7 ds if small sample (< 1mg/ml).

then → Incubate at 37°C → redissolving.

then Cryoglobulin Conc. can be determined via spectrophotometric analysis.

Specific Immunologic Assays may be used to identify Cryoglobulin → Components (Igs, Light chain & clonality).

② Histopathology & DIF :-

- * Papular lesions → LCV (SVV).
- * Ulcerative " : → Medium sized vasculitis.
- * Granular: C3, IgM (أكثر تعبير) at BVs.

عشان كده لبعض بيصيبها (Small-med) عادة

ANCA Vasculitis

(23)

def. of ANCA: group of antibodies (mainly IgG) against Antigens in Cytoplasm of Neutrophils & monocytes.

Types of ANCA: (Acc. to their staining Pattern):

1- **C- ANCA:** (Cytoplasmic ANCA) (CP)

- Antibodies directed against Proteinase 3
→ (PR3) Ag → granular Cytoplasmic staining.

(another Ag: Lactoferrin, Cathepsin G, Elastase)

2- **P- ANCA:** (Perinuclear & Nuclear ANCA) (PM)

- Antibodies directed against Myeloperoxidase
→ (MPO) Ag → perinuclear staining.

3- **X or Atypical ANCA:-**

- Antibodies Neither directed against (PR3) Nor (MPO). [another Ag]
- Diffuse Cytop. & Perinuclear.

Detection of ANCA:-

① first → IIF if +ve do:
② ELISA (Confirmatory).

لسهولة الحفظ

- WG → C- ANCA
- CSS → P- ANCA
- MPA → Both (P ANCA > C-ANCA) (MPAN)

other dis: SLE, RA, IBD - chr. inf.

تفصيليا (HL)

- WG < 80% C-ANCA, 10 P- ANCA
- CSS < 60% P-ANCA, 10% C ANCA
- MPA < 60% P- ANCA, 30% C ANCA.

(24)

Vasculopathy:

- ✓ Vs wall infiltrated
- ✓ fibrin deposition & Thrombosis

We ← inflammation attempts to destruct (24)

A

Css phases

(A) (1st) ← Allergic Rhinitis
Asthma
Nasal Polyps
Periph. Eosinophilia

الأنف

(B) (2nd) Vasculitis ←

(C) (3rd) ← Allergic Rhinitis
Asthma
PN
HTN
Result to other systems ↘

Wegener's Granulomatosis (45ys)

- definition: syndrome consisting of Necrotizing granuloma of
  - RT (upper&lower) → otitis, Epistaxis, saddle, sinusitis
  - Kidney → Necrotizing GN
  - BVs → " Angitis

- CIP → ROUGH + Cut.
- ACR Criteria for Dx: (≥2)

Wegener's granulomatosis (WG)
1. Nasal or oral inflammation
2. Chest X-ray showing nodules, infiltrates (fixed) or cavities
3. Microscopic hematuria or red cell casts in urine
4. Granulomatous inflammation on biopsy (within vessel wall or perivascular)

Two criteria classify WG with a sensitivity of 88.2% and specificity of 92.0%

Pathogenesis:
- genetic PR3 (proteinase 3) positive polymorphonuclear cytoplasmic ANCA
- Staph → Nasal inflamm.

- Biopsy ? بايوبسي

Tx: Cs + Cyclophosphamide
Cs + MTX
Rituximab
Septrin (↓ relapse of Inf.)

Manifs → ROUGH

Ut. manifs (40%)
- LCV
- Urticaria
- Purpura
- Petechiae
- PG.
- Papulo-Necrotic lesions at Elbow → ulcerate
- Gingiva: red, friable, Hyperplastic

Radiographic Abnormalities of CXR (Nodules-Cavities-infilt).

Nasal & oral ulcers

Urinary Sediment (RBCs, casts) - Hematuria.

Granulomas of lung/skin

Hemoptysis.
others: Cough, Dyspnea, chest pain.

IPSY (Pathognomic)

Churg Strauss Synd (CSS). (♀, 35ys)

(Allergic granulomatosis or Angiitis).

CIP: (6)
- Asthma
- Eosinophilia
- sinus Abnormality
- PN
- Pulm. infilt.
- Perivascular Eosinophils on Biopsy.

ACR Criteria (≥4 → ♦ diagnostic)

- Cut. (55%): → ++
- P: Purpura (++)
- S.C Nodules (+)

others ± Granuloma

Commonest cause of death:-
Myocarditis & HF
other manifs: CNS, CVS, Musculosk, ocular, cut. (↓↑)

→ May be drug induced:-
- Azithromycin
- HBV Vaccine
- Zafirlukast

Path:
- Eosinophils & Extravascular granulomas.
- Necrotizing vasculitis of small and med sized.

Purpura, Nods

Papulo necrotic lesion: Eos. absence, Palisaded Ex granulomas

Eos. Cationic protein.

(HL) **Differentiate bet. WG & CSS**

(1) Granuloma (3) Asthma, Eosinophilia, Granuloma

	Wegeners	Churg Strauss
(E) Asthma	−	+
(E) Eosinophilia in Blood	−	+
(E) perivascular Eosinophils on Biopsy	−	+
(2H) Hemoptysis	+	−
(2H) Hematuria	+	−
. C-ANCA	80%	10
. P-ANCA	10%	60%

(E) عيوة عنزة

Microscopic polyangiitis (MPA)

- Commonest ANCA Type
- No granuloma
- No Asthma
- Kidney is the most Commonest

Dermo pulmonary renal Synd.

✓ Commonest ANCA Associated Vasculitis

✓ Commonest organ affected is: Kidney

~50 Ys

M > F

. CIP .
- fever
- Arthralgia
- Myalgia

→ may appear ms-Ys before Explosive phase of the dis.

Most Common ← Type ANCA organ Kidney

O
- No Asthma
- No Eosinophilia
- No Granuloma

X

△
- Neuropathy
- G.N (80% → Necrotizing GN)
- pulm. involvement & Hge

. Skin manifs : purpura, Erythema & urticaria, Nodules, Ulcers & Splinter Hge.

. ANCA = P-ANCA (60%) > C-ANCA (30%)

GN — PN — pulm

(Hl) Cs, Cyclophosph, others.

De

Medium Sized Vasculitis (2016)

A- PAN → HBV

B- Kawasaki

(Pg ~ 150 ls)

(A) PAN (Polyarteritis Nodosa)

- Def: Necrotizing Vasculitis affecting Small-Medium sized arteries Commonly: Segmental

branching points → ⊙ Coronary ⊙ Hepatic ⊙ Renal ⊙ Cut. → Classically at their branching Points → Aneurysmal dilatation (and)

- Age: ~40-60 ys. Children.
- Sex: (M) F 4:1
- Association: classical associat :-

(classic) → Systemic Type → HBV (+)

(Bg) → Cut Type → Skin inf ; ?HCV !? → HIV

Other 2ss (2 Types) → FMF, SLE, IBD

- Treatment
  - ↓ of inf. → stop the drug
  - NSAIDs
  - Cs + Cyclo / Azathi + Antivirus
  - MTX
  - Dapsone
  - other Immunosuppressive in.

Types 1- Bg Cut. (10%)

"classical Type" → 2- Systemic. (affect muscular a.a of vital organs).

- CIP: A. Systemic Type (90%)

* systemic Manifs: FAHM myalgia Wt loss fever N-sweat
  - Mononeuritis Multiplex
  - CHF
  - Renal: HTN & RF.

* Cut. manifs (50%) → Usually Livedo reticularis & (LR) Nodules & Punched out ulcers

(B) Cutaneous Type (10%)

→ More in children (BA) ~U
→ mild & self limiting

. usually affects the L.L: Livedo Retic. / painfull S.C Nodules & punched out ulcers -

Histopathology: Segmental Necrotizing Vasculitis at branching points → Aneurysmal dilatation.

ACR for diagnosis: (3/10)

- Wt loss > 4 kg
- Livedo Retic.
- Pain: Testicular pain / Ms or leg pain
- HTN
- PN
- Lab: ↑ BUN (or) ↑ S. Creat.
- +Ve (HBV)
- +Ve Arteriogram → Aneurysm or occlusion.
- +Ve Biopsy.

Rx:

① HBV: Best → IFN α + Vidarabine
② CS ± Cyclophosphamide.
③ Rituximab (or) IVIG.

DD → EN

Kawasaki Disease (Mucocutaneous LN syndrome)

Def: Type of medium sized vasculitis characterized by Coronary vasculitis with non specific cutaneous manifestations

Etiopathogenesis: ?? 1-Genetic, 2-Autoimmune 3-Toxin-Mediated Super Ag — Staph, Parvovirus B19

Kawasaki Disease Diagnosis Criteria

knowmedge

Mnemonic: "CREAM"

Criteria

Fever >5 days

Fever >38°C not responding to Antibiotics

+

4 out of 5 of the following

C	Conjunctivitis (non-exudative)
R	Rash (polymorphous non-vesicular)
E	Edema (or erythema of hands or feet)
A	Adenopathy (cervical, often unilateral)
M	Mucosal involvement (erythema or fissures or crusting)

Intellectual property of Knowmedge.com

Fever + CREAM

Rash specially (perineal) (May be early Manifs) → easily desquamate

Methods- Classification

Complete KD:

- 4 clinical signs (CREAM)
- Fever for at least 5 days

Incomplete KD:

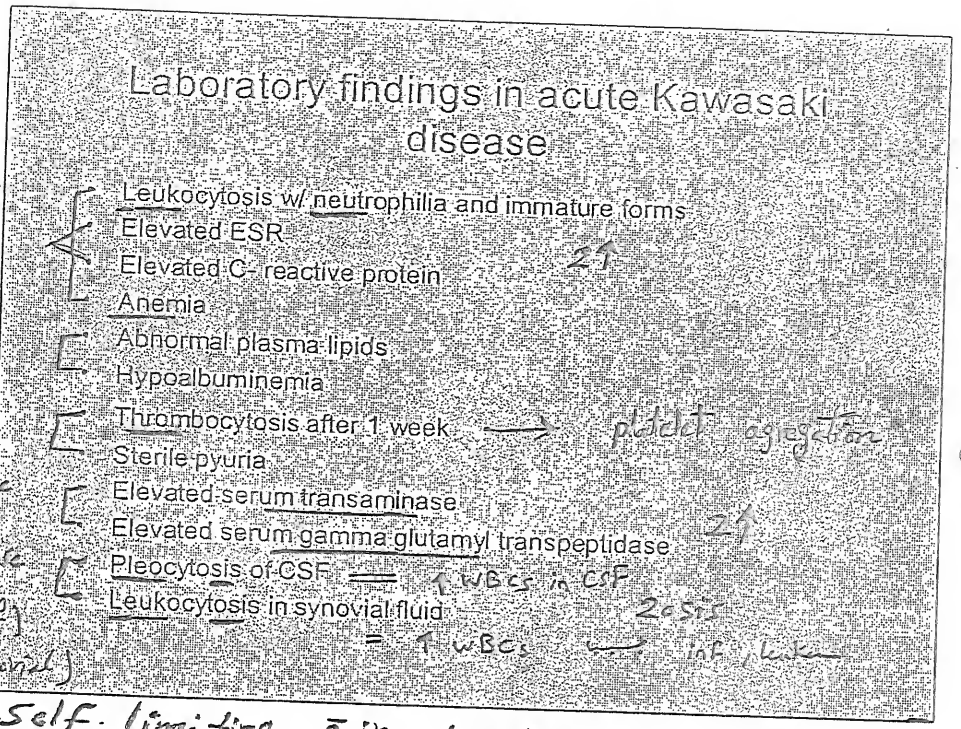
- 2 or 3 clinical signs
- Fever

All patients received standardised treatment and follow up → c/o أخلاف

- **Clinical:** Criteria & BCG scar reactivation/inflammation ← HP
- **Two-dimensional ECHO or coronary angiography**
- **Lab.**

التقرب مكان تطعيم BCG

NB cut HP → Non specific Pathology.



1- CBC ↑ L N A

2 ↑ ESR CRP

plasma lipid ↓ albuminemia

sterile pyuria

3 ↑ Sr. Transaminase ɣ glutamyl Transpeptidase

pleocyt (CSF)

leukocyt (synovial)

Anemia leukocytosis neutrophil

CBC

↑ ESR

↑ CRP

↑ Sr. transaminase

↑ Sr. ɣ glutamyl tr peptidas

↓ Albuminemia

plasma lipid AL

pleocytosis CS

leukocytosis Syno

Thrombocytosis

sterile pyuria

= urine analys

- Self. limiting ē in 1-3 Ws
- 25% → Coronary aneurysm → Thrombosis & MI (MR 2%)

NB - Rash + fever لازم تتوقعي كاوازاكي

- become the Most Common Acquired Heart dis in children after Rheum. fever.

DD: SSSS, TSS, Exanthema, EM & DE.

[HH]

① Aspirin (Thrombus ضد) 80-100 mg/kg

لتقسيم على جرعات يوميا طلة بيوميه أو بعد يوميه سم نزول الحرارة

→ Maintenance 4 mg/kg/d For 6-8 Ws

بديل لأي تناطر ع الأطفال (Clopidogrel)

② IVIG (Aneurismic ضد) 2gm/kg/12hrs

تنفذ ميا ته

لازم يدي على مدار ١٢ ساعة جرعة واحدة فقط

Alternative to IVIG:

- Pulse MPA (CS)
- Infliximab
- Ulinastatin إنزيمات (Protease inhibitor)

Large Vs Vasculitis

(31)

• Giant (Temporal) Cell arteritis [Horton's dis] — >50y

- of granulomatous Vasculitis of Aorta, its Major brs & Medium sized Vs. specially Extra-Cranial brs. of Carotid the Temporal a. (Head & Neck)
- pt >50 Ys (♀>♂)
- Etiopath: IFN-γ (by T cells) → ++ Multinucleated giant cells & Macrophages → factors → myofibroblast prolif. → Intimal Hyperplasia → arterial lumen occlusion
- C/P
  1. Systemic: Headache, Earache, Sore throat, Jaw Claudication
     - ← Blindness.
     - ← Pain & stiffness of Pelvic & shoulder girdle
  2. Cut (rare) = Tender, Nodular, swollen, Indurated, pulseless Temporal artery.
- Tt: (Cs) ± (MTx)

• Takayasu arteritis — <50y

- Granulomatous Vasculitis of aorta & Major brs that affect pt <50Ys
- (Aortic Arch Synd = pulseless dis.)
- Etiology: Inf. TB & Viral; Genetic; Autoimmune
- C/P
  1. Prepulseless phase: fever, wt loss, arthralgia (< wt loss, Fever, Arthralgia)
  2. Pulseless phase:
     - Bruit, No Pulse
     - ← Irregularity of BP bet arms & legs.
     - ← HTN, Headache, Angina, Seizures,
     - ← Retinopathy
  3. Skin lesions
     - Early: EN or EI like
     - Lat: PG like
- HP of Skin:
  1. Granulomatous Vasculitis
  2. lobular & septal Panniculitis +
  3. Fat Necrosis.

Vasculopathy

1- Degos dis.

2- Erythromelalgia.

Chr. of vasculopathy:-

i. Fibrin deposit or thrombosis ± acut vascular inflamm.

ii. Vs wall infilt. ± acut alterats

iii. ± other features.

1- Degos dis (Malignant Atrophic papulosis)

Def Autoimmune Vasculopathy causing occlusion of Small & Medium sized arteries in (4) systems ← skin, GIT, CNS, Eye → (Ischemia)

Etiopathogenesis: unknown ± d.t

1. Genetic: ?? AD
2. Autoimmunity
3. Viral inf.
4. disturbed clotting system.

→ All (+) → Endothelial defect ± Impaired platelet + Fibrino lytic activity & C5

Hematological / Endothelial / Clotting dis. ± C5 defect

[Not Considered Vasculitis as there is no arterial Wall injury & No Immune Complexes]

Epidemiology: Age: Young adults

Sex: M>F (3:1)

Clp (1) Cut lesions [precede the systemic lesions by yrs]

- 30-40 Asympt, Small sized (2.5mm) dome-shaped papules → become Necrotic & Umbilicated → heal ± porcelain White Scars surrounded by Telangiect.
- Site: Mainly at trunk [back] & limbs.

2 forms → Cut / systemic

2- GIT lesions: → Acute abd pain, Bleeding, perforation → death. [Cause of death] [50% in 5 yrs]

(33)

3- Nervous (CNS) lesions: stroke, Headache, Epilepsy, ...

4- Eye: diplopia & visual defects.

Path → Epid: Atrophic ± some hyperkeratosis
Dermis: Wedge shaped alteration (Edema, mucin, sclerosis & Necrosis)
Vascular: damage & Thrombosis

Tt: ① Cut. lesions:
- Antiplatelets < Aspirin / Dipyridamole
- IVIG

② systemic dis: → anti C5 (→ its activation)
- Eculizumab (approved for PNH)
- Treprostinil (SC) (" " pulm HTN)

DD: Dego's like in AICTDs & APLS.
LSEA.

→ Guttate Morphea
→ Lichen sclerosis et Atrophicus

(34)

Erythromelalgia
(Erythromalgia)

- Erythro = redness
- Melos = Limb
- Algos = Pain

(34)

- **Def.** Episodic attack of: Hotness, redness, burning Sensation at palms & soles that ppt. by warmth & hanging down & ↓↓ by Cooling & limb Elevation. → at night

- **Etiopathogenesis:** → unknown; there are 2 Types.

- I: Thromcy
- II: 1ry
- III: asse other than thrombo.

1ry (Idiopathic)
↓
- Genetic Mutation in Voltage-gated (Na_v) channel → ↓ threshold & ↑ hyper Excitability of Pain Neurons.

2ry

A — Thrombocythemia ass. (Platelet show ↑ No & dysf → Microthrombi)

B — Non thrombocythemia ass. ± asse
- Myeloprolif disorders
- DM (Diabetes)
- PVD = peripheral vascular dse
- Vasculitis
- AICTDs. (SLE)

- **Epidemiology:** . Age: Childhood - Adulthood
  . Sex: F > M.

- **Clp** مع لسعة أو زلة كهربائية بعد (٣) سنوات - حرقان - احمرار
غالبا في القدم (٩٠٪) أو في اليد (٢٥٪) يحس فجأة بالليل (كأنه حرق مستمر)
وتفضل طول الليل ويمكن يصحيها من النوم. يخف مع البرودة أو رفع القدم والليد

- **NB** ∴ 2ry (thrombocyt.) : ± (unilat) & ± → ischaemia. نقص

- **Exacerbating factors:** ① ↑ temp. ② hanging down ③ Walking or standing

- Path: ✗ → Biopsy (not) required & Non specific.

~~D.D~~:
- Autonomic dysreg.
- AET ??
- Pth: injury / surgery

1- chr. regional pain synd (reflex sympathetic dystrophy & causalgia)

نفس أعراض وكلاريا: بتبقى مستمرة
وليس لها علاقة بدرجة الحرارة.

2- P.N = may cause Tingling & Numbness (ك diff → Nerve Conduction study)

3- CCB & PV occlusive dis. (PVD)

NB → لازم تكلم بالأول إلرين لأنه ممكن يعرفه ٣ سنين
Myeloprolif. dis عنده

Treatment (كيف)

1- General: ارفع رجليك وبيك + تبريد الأطراف [Cooling, leg elevation

2- Thrombocythemic ass. type → (aspirin) ←

3- Other Lines:-
- SSRI.
- Gabapentin.
- CCB
- Tryptizol
- Capsiacin (lotion) (↓ pain)
- Nitroprusside
- PGE,
- Lidocaine
- opiates
- Epidural anaesthia

Livedo Reticularis

Def: Reticulated vascular pattern ⓦ usually representing ↑ vaso-spastic response to cold (but ± dt underlying systemic dis.

CAUSES OF LIVEDO RETICULARIS	
Congenital livedo reticularis	
✓ Cutis marmorata telangiectatica congenita (Vascular Malformat-) CMTC	
Acquired livedo reticularis	
(1) *Vasospasm* (Most Common Cause):– (VC)	= cold
• Cutis marmorata/physiologic livedo reticularis	◦ Idiopathic (ity) ◦ physiologic (CM)
• Primary (idiopathic) livedo reticularis	
• Autoimmune connective tissue diseases (e.g. SLE)	◦ AICTD. ◦ RayN.
• Raynaud's phenomenon/disease	
(2) *Intravascular/reduced flow*	
⊙ Increased normal blood components : (↓ Bl. flow) ↑ Coagul, ↑ Bl. Count, Abn prot	◦ thrombocyth ◦ PCV ◦ APS. ◦ DIC ◦ Cryoglob. ◦ cryofib. ◦ protein S & C ◦ para protinemia
– Thrombocythemia	
– Polycythemia vera	
TTP	
⊙ Abnormal proteins :	
– Cryoglobulinemia	
– Cryofibrinogenemia	
– Cold agglutinins	
– Paraproteinemia	
⊙ Hypercoagulability :	
– Antiphospholipid syndrome ✓ APS	
– Protein S and C deficiencies	
– Antithrombin III deficiency	
– Factor V Leiden mutation	
– Homocystinuria, hyperhomocysteinemia	
– Disseminated intravascular coagulation (DIC)	
⊙ Thrombotic thrombocytopenic purpura	
(3) *Vessel wall pathology* (Vasculitis / Livedoid) (calciphyl. / Sneddon's) (4)	vasculitis (Med) ON Wrap; Sneddon's Syn; Calciphylaxis; livedoid vasculopathy
⊙ Vasculitis (Medium sized) ← PAN, Cryglob.	
– Cutaneous polyarteritis nodosa	
– Systemic polyarteritis nodosa	

CAUSES OF LIVEDO RETICULARIS

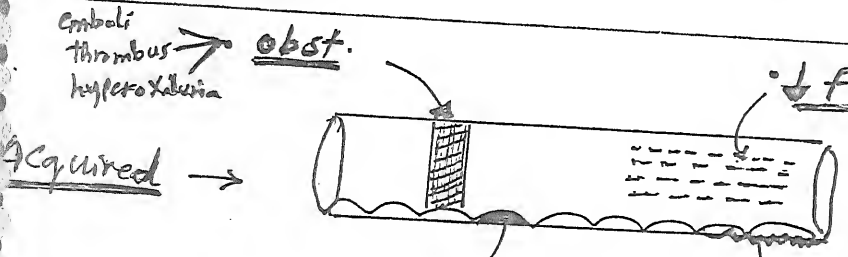
- Cryoglobulinemic vasculitis
- Autoimmune connective tissue disease-associated vasculitis (e.g. rheumatoid arthritis, SLE, Sjögren's syndrome)
- Calciphylaxis
- Sneddon's syndrome
- Livedoid vasculopathy (also intraluminal obstruction)

Vessel obstruction

- Embolic
  - Cholesterol emboli
  - Septic emboli
  - Atrial myxoma
  - Nitrogen (decompression sickness)
  - Carbon dioxide arteriography
- Thrombosis (see above)
- Hyperoxaluria

Other

- Medications (e.g. amantadine, norepinephrine, interferon)
- Infections (e.g. hepatitis C [vasculitis], *Mycoplasma* [cold agglutinins], syphilis)
- Neoplasms (e.g. pheochromocytoma)
- Neurologic disorders (e.g. reflex sympathetic dystrophy, paralysis)
- Moyamoya disease



- Others :
  - Drugs → IFN, Amantadine
  - Inf → HCV & ...
  - Neopl. → pheochromocytoma.
  - Neurolog → paralysis.
  - Moya Moya dse

(CMTC) ← Cong ما تنساش

Livedo Branching

Types

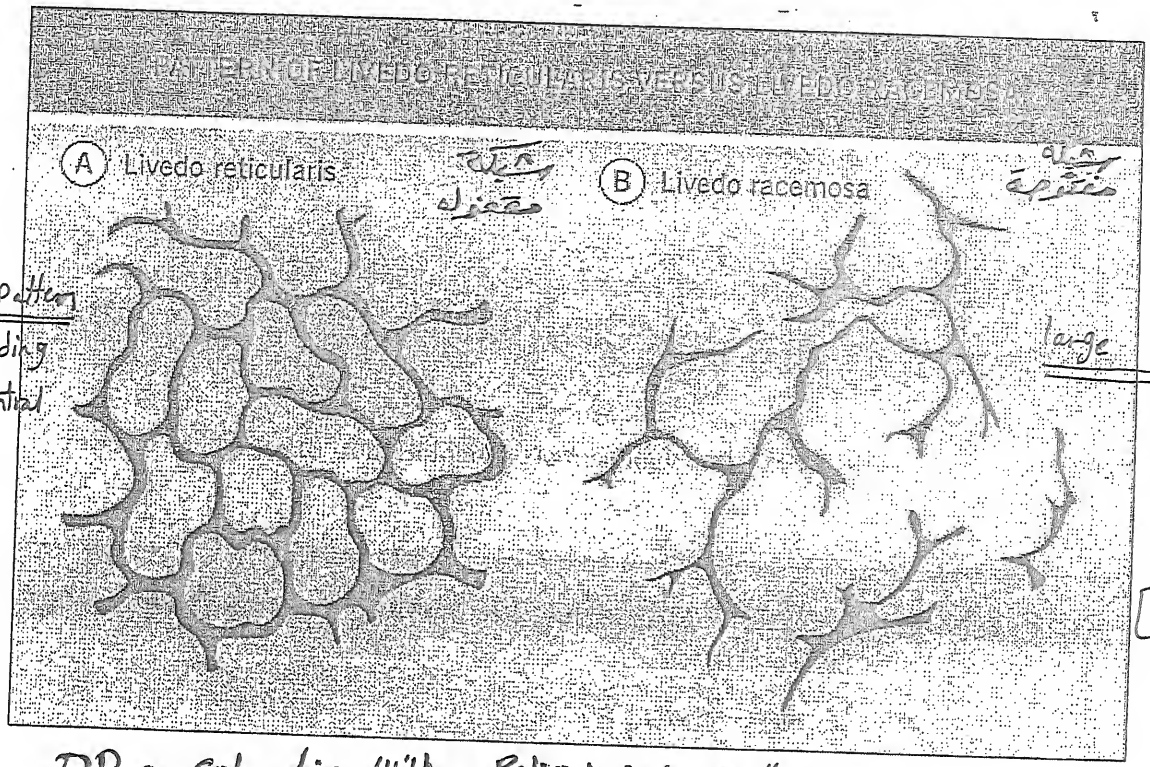
- Physiological LR: Transient (يختفي بالتدفئة)
- Other causes of LR: → persistent.

① **Livedo Reticularis :-**

Cyanotic (reddish-blue) cut. discolorat~ surrounding Pale Central area.

② **Livedo Racemosa :** distinct pattern of LR consisting of large branching pattern that usually occurs on Trunk & Proximal limbs.

- Most Common Cause: Sneddon's synd. but ± Caused by: APS



closed pattern surrounding pale central area

large branching pattern [opened]

[APS
[Sneddon's

- DD : Cut. dis with Reticulated Patterns

1- **Erythema ab Igne :**
   - a- reversible LR like (then)
   - b- fixed reticulated hyperpigmentat~

2. **REM synd** (favors central trunk)
3. **Erythema infectiousum**
4. **Poikeloderma**
5. **MF**
6. **GVHD**

→ Epidermal changes on pathology

Livedoid Vasculopathy

(Livedoid vasculitis, Atrophie blanche, Livedo reticularis with summer ulceration, Segmental hyalinizing vasculitis)

- Def: chr. vascular disorder ch BY (2) stages
  1- Persistent painful ulcers of Lower Legs. Healing
  2- Atrophie blanche scars
- Etiopath. (Types): 2
  1- Idiopathic (Dy)
  2- 2ry Types: Thrombosis (Coagulopathy ← platelet fibrinolytic protein defect etc), chr. Venous insuff ē Venous HTN, VV, (APS), SLE.

C/P: 2 components:

1- ulcers: Painful, punched-out on A background of Retiform purpura or Livedo Retic. (Now Named) (Livedoid vasculitis) around Malleoli

2- Atrophie blanche scar: which is characterised by:

ⓐ Star-shaped or polyangular, ivory white depressed atrophic plaques

ⓐ Prominent red dots within the scar due to enlarged capillary blood vessels

ⓑ Surrounding pigmentation. or Telangiect.

Pathology: The characteristic histologic findings in livedoid vasculopathy are mild perivascular lymphocytic infiltrates and extravasated red cells surrounding superficial dermal vessels with hyalinized walls and luminal fibrin deposition. ext. RBCs

Differential diagnosis

DD: 1- Other causes inflammatory retiform purpura (see Ch. 23).

2- Other causes Atrophie blanche: Atrophie blanche-like lesions are not specific for this syndrome, so that a history of the characteristic ulcers should be used to distinguish this form of skin injury from other disorders that can lead to atrophic scarring, *such as* APS, CSVV, sickle cell anemia, hydroxyurea-related leg ulcers, Diabetic vascular disease, Any injury to the skin of an ageing lower leg, such as following cryotherapy or curettage and cautery in the treatment of skin cancers, and **especially** venous stasis with varicosities

APS
CSVV
SCA
D.M
Injury ← Cryo, Cautry, Curettage

Treatment :

1- * Antiplatelet, anticoagulant and fibrinolytic therapies[53]. (Aspirin)
2- * Anabolic agents such as danazol and stanozolol.
3- * PUVA therapy[55].

* In patients with atrophie blanche-like lesions and lupus (SLE) antimalarial drugs may be helpful.
*Patients on hydroxyurea with atrophie blanche-like lesions may need a trial off the drug, since hydroxyurea may mimic this syndrome through unknown mechanisms.

Pigmented Purpuric Dermatoses
(capillaritis; purpura progressive pigmentosa)

(Jan 2010)

Def: Group of chronic diseases of unknown etiology characterized clinically by petechial hemorrhage and histopathologically by lymphocytic capillaritis. They are not associated with any systemic findings.

Etilogy and Pathophysiology: The etiology is unknown. However the following may play a role:

* Venous hypertension
* Gravitational dependency
* Exercise
* Genetic predisposition *(familial cases of Schamberg disease and Majocchi disease have been reported).*
* Drug.

They are not associated with any systemic findings or coagulopathies.

Epidemiology: -Age: * Schamberg → any age.

* Majocchi and Lichen aureus → children or young adults.
* Eczematidlike purpura and the pigmented purpuric lichenoid dermatosis → middle-aged men (40-60).

- Sex: All M > f except Majocchi (F>M).

-Race: no predilection.

C/P: -There are 5 classical types:

1- Schamberg's disease *(progressive pigmentary dermatosis).*
2- Majocchi's disease *(Purpura annularis telangiectodes).*
3- Pigmented purpuric lichenoid dermatitis of Gougerot and Blum.
4- Eczematid-like purpura of Doucas and Kapetanakis *(itching purpura)*
5- Lichen aureus *(lichen purpuricus).*
6- Other rare types: (A) Granulomatous (HL) (ROOK) (B) Familial (C) Linear and quadrantic → Pigmented purpuric Erupt.

(44)

NB: Many consider itching purpura and eczematidlike purpura to be variants of Schamberg disease

* Clinical features: All cases Ch. By:
  - → Orange-brown, speckled, cayenne pepper–like discoloration (due to hemosiderin deposition)
  - → Usually affect lower legs and ankles, however any site can be affected even the face and palmoplantar.
  - → Usually asyptomatic except itchy purpura which shows severe itching
  - → Have very chronic course.

1-Schamberg's disease: any age / ♂

- Most common type.

- Lesion: *patches or Plaques:* red – brown with pinpoint 'cayenne pepper' macules (represent petechiae) usually bilateral at lower legs and ankles but can also occur on the thighs, buttocks, trunk and arms (however a unilateral distribution is occasionally observed. Over time, the lesions become darker brown in color and then fade, but new crops often subsequently appear.

bilat patches (Red brown) → dark brown → fades → (Recurrence)

petechia + Telangectasia

child ♂ 2- Majocchi disease or Purpura: *Annular Plaques*: 1–3 cm in diameter with punctate telangiectasias and cayenne pepper petechiae in the border.

NB: A variant termed purpura telangiectatica arciformis (Touraine) consists of fewer, larger and irregularly arciform lesions.

middle age ♂ 3- Pigmented purpuric lichenoid dermatitis of Gougerot and Blum: (rare): Lesions similar to those of Schamberg's disease but there is characteristic purpuric red-brown lichenoid papules and can involve UL and LL.

middle age ♂ 4- - Eczematid-like purpura of Doucas and Kapetanakis *(itching purpura)*: similar to Schamberg's disease but differs in: (Rapid - Extensive - itchy)

* Persistent intense itching
* More extensive
* Develops more rapidly.

- ~~Lesions: scaly petechial or purpuric macules, papules and patches often with a~~
- DD: 1-Carbromal sensitivity, and less commonly with other drugs such as meprobamate, carbamazepine and perhaps even some foods.

2-Clothing or rubber dermatitis may produce a similar picture.

child ♂ 5- Lichen aureus *(lichen purpuricus):* Ch. By:

- More localized
- More intensely purpuric

Hemosiderin from RBCs extrav.

Def. Clusters of petechial Age ē chic HP of.

1. Schamberg: patches & plaques, red. brown ē cayenne pepper-like dots (petichae) → Fade ē dark brown Colors → exacerbat↔ remission.
2. Majocchi → annular plaques ē Petichae & punctate Telangiect ✓
3. L. Aureus → solitary, chr. plaque ē rusty Color ± surrounded by orange Hue.
4. Itching. P. → as schamberg but Rapid, extensive & itchy

- Lesion: solitary, chronic patch or plaque with rust to purple-brown color but may have a golden hue.

6- Other rare types:

A- **Granulomatous pigmented purpuric dermatosis** : An uncommon variant of pigmented purpuric dermatosis has been reported in which there is granulomatous histology.

B- **Familial pigmented purpuric eruption:** rare AD familial inheritance in some cases of Schamberg and Majocchi . Discrete reddish-brown spots develop in childhood or adolescence but of larger size than in Schamberg's disease and are arranged in a mosaic pattern. The lesions gradually cover a larger area and involve new sites, mainly on the limbs and in the larger flexures, but there are no symptoms.

C- **Linear and quadrantic pigmented purpuric dermatoses** : Various morphological types of pigmented purpuric eruption may occur in a linear or zosteriform distribution , or less commonly may diffusely involve a single quadrant of the body.

Investigations: thrombocytopenia and vasculitis should be excluded because of the purpuric (usually petechial) nature of the lesions and clinical misdiagnosis:

1- CBC, coagulation profile, Hess test for capillary fragility.
2-Histopathology: in all cases there are Capillaritis:
1- RBCs extravasation,
2- Endothelial cell swelling,
3- Perivascular infiltrate of lymphocytes and macrophages is centered on the superficial small blood vessels.
4- Hemosiderin-containing macrophages:
5- Mild epidermal spongiosis and exocytosis of lymphocytes may be seen in all variants except lichen aureus, which shows : a bandlike (Lichenoid) infiltrate separated from the epidermis by a thin rim of uninvolved collagen (Grenz Zone).

2- Dermoscopy has been reported to be a useful tool for assisting the clinical diagnosis of pigmented purpuric dermatoses.[12]

NB: Histochemical staining with Perls stain (to demonstrate iron or hemosiderin) and Fontana-Masson stain (to exclude melanin pigment) may be helpful. Hemosiderin deposition in the dermis is more superficial in pigmented purpuric dermatitis than that seen in stasis dermatitis, which is a useful differentiating feature.

Differential diagnosis :

The clinical picture is often sufficient for diagnosis, but a biopsy specimen may be required to distinguish them from:

- Lichenoid variant from small vessel vasculitis.
- Angioma serpiginosum (but unilateral).

- MF (هنا early stages may closely mimic a pigmented purpuric dermatitis both clinically and histologically) → extensive Schamberg above Knee
- ACD (e.g. due to rubber or azo dyes such as Disperse Blue),
- Nonallergic reactions to topical medications (e.g. fluorouracil or eutectic mixture of local anesthetics [EMLA]).
- Drug eruptions (e.g. carbromal, meprobamate, acetaminophen, infliximab, pseudoephedrine),
- Suction-induced purpura (e.g. cupping or pressing the back against a bathtub)
- Hypergammaglobulinemic purpura of Waldenström.
- Dermal hemorrhage secondary to venous hypertension, which presents with petechiae superimposed on diffuse hemosiderosis (Fig. 23.5B) rather than the discrete yellow-brown background patches that characterize Schamberg's disease.

Treatment

1- Instructions: Avoid prolonged leg dependency and treat the underlying venous stasis. by compression hosiery (أفضل علاج)

Supportive: leg elevation, elastic stocki, Avoid leg depe

2- Medical ttt:

- Topical CS : helpful, especially if there is pruritus or marked erythema.
- Ascorbic acid (500 mg twice daily) and rutoside (50 mg twice daily) → SUCCESSEFL
- NB-UVB and PUVA (2008-2009). فعالة
- Griseofulvin (Tamaki et al; *Br J Dermatol.* Jan 1995)
- Cyclosporin.
- Colchicine.

Medical: vit c, rutoside, cs, Colchicine, Cyclosporine, Griseofulvin, PUVA, NB-UVB

Ruta c 60mg مرتين

vit c 1gm +

Vascular Tumors

classification

1. **Reactive:**
   - PG = Pyogenic granuloma
   - ALHE = Angiolymphoid hyperplasia ē eosinop

2. **Malformation:**
   - Cap Malformation (CM) → PWS, SP (Salmon patch)
   - Venous ~ (VM) → Venous leake, Blue Rubber Blat
   - Arterial ~ (AM)
   - Lymphatic ~ (LM) → Lymphangiom circum
   - Angio Keratoma
   - Mixed Malformation
   - Verrucous Heamangioma
   - AVM
   - Angiomaseppigenosum

3. **Bn Tumors:**
   - Infantile Haemangioma (IH)
   - Cong ~
   - cherry Angioma

4. **Border line = low grade Mg:**
   - Kaposi Sarcoma

5. **Mg Tm:**
   - Angio Sarcoma

6. **Perivascular Neoplasm & Neoplastic like Conditions:**
   - Glomus Tm
   - Glomangioma

7. **Telangiectasia.**

ALHE = Angiolymphoid hyperplesia ē eosinophilia

Def: Ben or low grade Mg T-cell proliferation ē 2ry vascular prolifera ch' by

clinically

- Papule, Nodule, plaques

(2D) [Dome shapped
[Dermal

[Isolated → may be grouped
[Reddish - pink

Site → Scalp s Neck, face (periauricular)

B →

ALHE = **Pseudo pyogenic Granuloma**

rarely site - LN, Mouth, Tongue
Bone, Testis

Histopathological

→ Endothelial cell proliferation ± Eosinophilic infilt

→ **Endothelial cell** have 2 ch''

- large epithelioid or Histoid
- Vacculata cytoplasm

NB Peripheral Eosinophilia 20%

tt:

- Surgical
  - Laser
- IL-cs
  - Indomethacin
- Isotretinoin
  - Imiquimod
- Cryo
  - Electro
- PDL

Kimura's dse

Def B-cell proliferative disorder ē 2ry vascular proliferation

affect: Skin, LN, Salivary gland → S.C painless skin lesion

[periauricular - parotid - sub Mandibular]

ass ē L.N < Single / Multiple & Salivary gland

affection at same site or distant

Path:

- Lymphoid follicles & Bl-Vs proliferation ē **Hobnail** endothelial cells
- Marked Eosinophilia

~~DD~~ : from ALHE

inflamm → 2ry vascular proliferation

ALHE	Kimura's
→ Vs proliferation é 2ry inflammation	⊙ Inflammation → 2ry Vs prolif
[Western الست الغربية O+ > O→	[oriental الرجل الشرقي O→ > O+
- Bn , low Mg T Cell Proliferation	- B cell inflamation ds é 2ry Vs prolif
[Dermal Rare extra cut affection	- deep S.C - affect ← skin, LN, salivary gland
— epithelioid / Histoid endothelial cells é Cytoplasmic Vaccules ± Eosinophilic infiltrate - T. cell type (H P)	- Hob Nail endothelial cell proliferation - Marked ++ Eosinophilic infiltrate → germinal follicles é eosinophilic folliculitis - B. cell type - less Vs proliferation
[peripheral Eosinophilia (20%) Normal IgE	[++ Eosinophilia (BL) ↑ IgE - fibrosis

Hob Nail Cells → bulbous (like) Nucleous é Nuclear projection to cytoplasm.

Nucleous big rounded

Pyogenic granuloma

def: Reactive vs lesion cli by rapidly growing, friable, red papule or polyp of skin or Mucosa that frequently ulcerate.

Misnomer ↔ No infectious agent
Not granulomatous

Tumor of pregn = **Eruptive Hemangioma** = **lobular Cap Hemangiom**

ot = o→

> child young adult

AE:

1- Reactive : to trauma – irradiation
2- Abnormality in bl. flow : PG in preexisting pws
3- Pregnancy
4- Drugs : sys Retinoids & Indinavir & Anti EGFR Ab.

C/P:

- Solitary (Red papule / polyp) – grows rapidly
→ Friable → bleed ē trauma → ulcerate
site → gingiva, finger, lips, tongue, face الأكثر صدوراً ثم الأقل
↳ ē preg
تسمى granuloma gravidarum.
- Rare eruptive or disseminated (Multible satellite lesions) توزيع الأورام

H/P:

- prominent epithelial (Collarettes) resulting from peripheral adenexial hyperplesia or downward growth of rete ridges bridged by Flattened epidermis. حواف, Lt Margins كوله
→ Well circumscribed, exophytic, Pedunculated proliferation of small cap – arranged in lobular pattern. تذكر أنواع

DD:

- bacillary angiomatosis
- Kaposi Sarcoma
- Glomus tm
- [illegible]

ttt:

[Surgery, Laser] [Cryo, Electro] [Sclerotherapy, Topical Tim

Vascular Malformation

- General ch: . at birth, (No) sexual * predilect, or gestational, slow (Expansion) proportionate ē growth & persist for life
- Any organ can be affected, but [Skin & MM] are commonest. ±
Associated ē deeper or Extra cut. involvement.

Classification (HL)

- Slow-Flow (early onset)
  - Capillary Malformation (CM)
    - SP
    - PWS
    - Telangiect.
    - Cutis marmor
    - Nevus Anemicus.
  - Venous Malformation (VM)
    - V. lake
    - Blue Rubber Bleb
    - Glomovenous malf.
  - Lymphatic Malformation (LM)
- Fast-flow (Latent)
  - Arterio-Venous Malformation (AVM)
  - Arterial Malfs. (AM)
- slow or Fast Flow
  - Combined Malformation
    - KTs (CLV)
    - Parkes Weber (CLV+A)
    - Mulliken (LV)
    - Proteus (C&V)

(PWS ليس)

Vascular Birth Marks

	Infantile Hemangioma	Vascular Malformation
Def.	Cellular proliferation (Tm)	Errors in vascular Morphogenesis
Epidemiology	More common in: premature, F > M (3:1)	(No) Gender or Gestational predilection
Lesion:	Not at birth (3-5 ws after birth) → rapid prolif. → Involution. Elevated	at birth → slow expansile proportionate ē growth → persistent. Flat. (↑ become Nodular ē Age
Pathology	Proliferating: Endoth. Hyperplasia, lobule formation, Mast cells, Prominent BM. Involuting: Fibrofatty replacement ↓ Mast cells	Depends on the Type: Ectatic irreg. V. channels. (NL Cell prolif = -Ve ki 67).
Immunohistoch.	GluT1 +ve, KI 67, FCεRII	all are (-Ve) (ki 67 → marker ↓ cell prolif)

Cap Malformations
- PWS
- SP
- Nevus Anemicus
- Telangiect

1 Salmon patch :

Nevus simplex = Medial Telangectatic Navus (MTN) = Fading Macular stain

- 40-50% Newborn
- irregular patches from Salmon pink to red color
- affects
  - glabella : Angel's kiss & Aigrette of forhead
  - occiput – Nape of Neck : Stark bite
  - Lambo Sacral : Salmon patch
  - eyelids – Nose

Fades by 1-3 ys → Reassurance

but Nape of Neck lesion → persist to adult 50%

- d2 dilitation of dermal Cap

2 Port Wine stain :-

Nevus Flammeus = Lat telangectatic Nevus (LTN)

3 Navus Anemicus :

~~DD~~

xx bl. flow

Vc & ↑ hypersensitivity to catecholamines

DiasCopy → fade of it's edge

(Hot – Minor trauma) → No change

Vitilgo → Smooth

glass - slide

Nevus depigmentosus

xx Melanin pig & Melanocytes

No change

✓ Erythema

Port - Wine Stain = Naevus flammus = LTN

cf = low flow cap Malformation

lp =

- Cong — Maybe aquired
- Flat — ~ raised ē ↑age (Nodular)
- Segmental — ~ localized

distributed at Trigemenal N branches (3) V_1 ophthalmic → {forehead, lower eyelid, upper ~.
V_2 MaXillary
V_3 Mandibular

- Bright-red patch that blanchié ē pressure.
- Face, extremeities never follow blasekho lines

→ Macrochelia → ↑ lip size (ناتج عن علو الدموية)

→ GNAQ Gene Mutation [encodes Gprotein α subunit]

clo - Indulation - irregularity - Thickening → ttt ē No effect (ملوش تأثير)
Should ttt as early as possible.

PWS assé

dis

1- Glaucoma
2- Neurological disorders { Motor, hemiplegia, seizures, MR
3- skeletal disorders → Spina bifida
4- Cutenous ~ (phakomatosis) jeté

1- Glaucoma + CNS dse ← MRI ē gadolinium, CT, SPECT, PET
- ass ē ophthalmic branch affection
follow up by eye examination Regurally
↑ risk ēin 1st 2yrs (30-50%)

2- Maxillary - Mandibular branch affection → ↑ growth of Lips - Tongue - Maxilla

Syndromes

1- Sturge-Weber Syn
2- Parkes-Weber Syn
3- Klippel-Trenaury Syn
4- Proteus synd
5- Megalo. encephalo-Cap Mali
- → PWS
- → persistant Salmon patch
- → Macro Cephaly
- → Asymm - overgro with

- Skeletal disorder :
  - Midline pws → lumbosacral, dorsal, Nape area

Hall Mark of Spinal dysraphism — ass ē

pit - dimple - sinus - cleft
tail like fibroma - lipoma hypertrichosis
Melanocytic Nevus - Congscar

US → 3-5 mon
MRI → most sensitive

- Cut - disorders

1- phakomatosis Pigmento-vascularis [PPV] = twin spotting
Cap Malf + Melanocytic or other Nevus

type 1 → CM + epid N
type 2 → CM + dermal Melanocytosis (±) Nevus Anemicus
type 3 → CM + Nevus Spilus (±) Nevus Anemicus
type 4 → CM + dermal Melanocytosis + Nevus spilus (±) NA
type 5 → ē Cutis Marmorata telangectesia Congenita (CMTC)
+ dermal Melanocytosis + type 1

2- phakomatosis Pigmento-Keratosis :-
Nevus Sebbaceous + epid Nevus + Spilus Nevus

3- Angio lipomas = asympt - non infiltrating
- May be underlying Cap Malformation ↔ trunk, Pelvic girdle
- Laser - Resistant Cap Malf (CM)
- Fake

NB: phakomatosis → inherated dse affect → skin, eye, CNS

PWS → أدوية
CNS : MRI - CT.
eye : examine Regularly.
Spina bifida : MRI.
phakomatosis : examine skin.

PWS associé Synds

1] Sturge - Weber synd :

(3) Cap Malf
- Skin → PWS
- Eye → glaucoma, Conj congestion, choroidal angioma (CH)
- CNS → Neurologic disorders → CT

(2) both ophthalmic & Maxillary affection.
both eye lids ∿.
- seizures ✓
- MR
- Hemiplegia

(1) X-ray → double contoured calcification (Tram-Track)

2] Klipped Trenaury synd :

△ (3)
- CM → PWS of LL ∿
- VM → Cong V.V
- LM → fluid filled cysts

- hypertrophy Bone, Soft tissue
- Limb asymetry ← gigantism, shrinkage = Scoliosis
- Cellulitis
- Thrombosis
- Embolism
- Cut-ulceration

(Clo)

3] Park - Weber synd :

as klipped + A.V Malformation → Thrill → asse (HF)

4] proteus synd : = Elephant man dse

(3)
- overgrowth bone, soft tissue
- Birth Marks [PWS ✓ - CT Nevus (cribriform hyperplasia) - epid Nevus]
- others
  - Lipoma
  - CT Nevus → ch
  - ch facies ← enlarged occiput, ptosis, Long narrow face, open mouth at rest, upturned
  - CALM
  - Choristomas of eye

5] hyperkeratotic CVM =

[TS - [Sturge-Weber syn - [Nevus Seb - Nevus + telangiectasia

Lymphatic Malformation

* Lymphangioma Circumscriptum (LAC)

def: Cong lymphatic Malformation localized to area of < skin / s.c tissue
d2 structural abnormality

C/P:
- Fluid filled cysts or vesicles
- discrete (or) grouped
- Smooth (or) Warty
- translucent → Red → blue black
  (Bloody filled)
- Frogspawn
- Axilla, Neck, Groin
- (±) Lymphorrhea

Tt:
- **Radical excision** الأفضل
- IL cs
  - Propranolol
- Laser
  - Cryo
  - Electro
- IL
  - hypertonic Saline
  - Pirfenidone
  - Doxycycline
  - Sildenafil

Invest:
1. **MRI**: to avoid Recurrance after excision
2. **Immunohistochemical**:

Lymphangioma	Hemangioma
Weak (+ve) VIII factor	(+ve) factor VIII endothe
discontinous Basal lamina	Multilayer Basal lamina, NL Bl.vs
Anti CD34 (-ve)	Anti CD34 (+ve)

هشيل قد ايه عشان تحدفين

Co:
1. Cellulitis like Reaction
2. Cervicofacial Bony distortion
3. oropharyngeal obst
4. Gorham-Stout = disappearance Bone dis
   = visceral lymph angiomatosis + osteolysis.

NB:

deep Cavernous lymphangioma
- deep form of LAC.
- extensive illdefined swelling.

Cystic hygroma
- Large cystic space
- Axilla & Neck

Sup Lymphatic dilitation

Cong Malformation

LAC

- Birth

aquired

2ry to ↗ radiation / ↘ Mastectomy

Lymphangectesia = Aquired lymphangioma

- Adult
- ē lymphoedema

Aquired lymphangioma = lymphangectesia = —

Lymphatic interruption: - cellulit - crohn's metasta

E: → Traumatic injury to previously Normal lymphatics: —

1- Radical Mastectomy.
2- Radiation from Mg.
3- Metastatic LN obst.
4- Scarring Processes ← Infilt. / Keloid. / scleroderma. / scro Fulo derma.
5- Rare Causes

♂ - Penile ← Transient after circumcission / Elderly → ēaut evidance of obst

♀ - ē Pregn
- Cirrhotic Ascities
- AbNL dermal structure & function ↗ Photoaging. ↘ steroids.

C/P: as LAC on back graund of lymphoedema.

H/P: Large dilated lymph vs ē Flat endoth. cells

Papillary / Reticular / deep (rare)

dermis

+

epid changes ↗ Acanthosis ↘ Hyperkeratosis

Abscent S.C muscle coated cisternae.

LAC ~~DD~~ by H/P

Tt: 1- Compression
2- locally destructive Methods
3- guard against inf

Venous lake :-

- bluish papule on (lip - oral cavity) & soft, compressable fill ē dependency

→ use sun screen

DD

- Mg Melanoma
- Kaposi Sarcoma

by dermoscopy

Clo

- Thromboembolism.
- IV Coagulopathy

lips → libial incompetence
check, Tongue → Abnormal jaw growth
pharyngeal → obst, sleep apnea
limb → under / over-growth
Joint affection
bone clo

DD

- deep IH
- KTS

Invest

Doppler US - MRI → extent of lesion, Nature
Blood tests → Coagulation

ttt

1 - Compression garment
2 - Aspirin
3 - Laser
4 - LMWH
5 - surgical
6 - sclerotherapy

followed by

Synd assē VM

Blue rubber bleb Naevus synd (Bean synd) = BRBNS

الجلد الرئة واحدة

widly disturbuted small dark blue papules and skin coloured compressable protuberances (rubber bleb)

Large VM

- **GIT** lesion → bleeds → Iron ↓ Anemia
- CNS
- Lung
- heart

less common

Maffucci Synd

① VM (blue to skin coloured)

② - Enchondromas

hamartomatous proliferation of chondrocytes → Abn ossification of diaphysis & Metaphysis

③ Cosmetic & orthopedic clo

site
- Extremities
- Cephalic lesion ← eye clo, CNS clo

Angio Keratoma

def : group of disorders ch' by

clinically

asymptomatic hyperkeratotic Vascular lesions

Pathologically

1 - Hyperkeratosis
2 - Sup papillary dermis Vascular ectasia
except circumscriptum Capi lymphatic Malfor
3 - dilated bl.vs

clp

- Soft
- Compressible
- pink-red

} Papules

3-5 mm
ē hyperkeratotic epid

Types :- [اختفظ النوع / الاسم / assē]

1 Angiokeratoma of Mibeili → extremities ± AD

- Bilat Symetrical → dorsum of Hand, Elbow, Knee

10-15 ys
o+ > o→

→ assē → Chillblains.
→ Acrocyanosis.

2 Angio Keratoma of Fordyce → genital

* Scrotum - Vulvae elderly **>50-60 ys**

assē Venous obst

o→
- Varicocele ✓
- Hernia ✓
- Prostatitis

Thrombophelibitis

- Sever bleeding ⓔ Minor trauma.

tt : Electro / Cryo

[3] Angio Keratoma Circumscriptum : AKc L.L ⑬

at birth – infancy – childhood (F) > m

clp papule { linnear / hyperKeratotic / verrocus } (±) BL, lymph filled cystic Nodules

site < L.L – foot / thigh – buttocks

ass ē { 1 → Navus flammus (pws) / 2 → Klippel T syndr / 3 → Haemangioma / 4 → Angiokeratoma of Fordyce }

D → H/R → lymphatic Component – Early age

[4] Soliatry Angio Keratoma :- L.L

at extremeties (L.L)

ass ē { trauma / Injury / irritation }

DD → Wart / M.M

[5] Angio Keratoma Corporis diffusum : = Fabry's dse

= Lysosomal lipid storage dse

e.t: XLR disorder ch' by deficiency of lysosomal enzy

∝ galactosidase A ↓

accomulation of glycosphingo Lipids (Ceramide Trihexoside)

in fluid, Visceral organs → endothelia / perithelial sm

Metabolic dse

Eye { Corneal opacity. / dilated Conjunctival Bl.Vs & Tor vis / upper eyelid oedema. } Constricti

clp الأول

Angio Keratoma (Skin)

↑ No – disseminated (Gro Rash) generalized, small size

less hyperkeratotic bathing trunk

() knee & umbilicus

Xerosis ——— Anhidrosis

Systemic

- Fever
- RF
- HTN
- CNS – CVS stroke
- → acroparathesia. (Sever pp burning pain) Parasthesia ē episodes (↑)

DD → fucosidosis

[5]:

1- Skin biobsy → ↓ dilated bl.Vs in upper dermis éch' ch' ↓ Vacculated endoth cell → lipid

2- Urine → (RF) albuminuria – Heamaturia – proteinuria – lipophages PAS (+ve) Maibeky like Cells → urinary section

3- ↓ ∝ Galactosidase A → in plasma – WBCs – Fibroblast

[6]:

1- Laser (Angio Ker...)

2- Aspirin (stroke)

3- Tegretol (pain)

4- Human Recombinant ∝ galactosidase A

5- Gene therapy

Treatment

(Ref: 2 · Bolognia · IH · IJDVL)

1. Reassurance: about Nature Course & Spont. Involut

2. Medical IH · (A) Topical
   - IL Cs
   - Topical Cs
   - Imiquimod
   - Becaplermin gel (DNNZ)
   - Easin (antiseptic & antiangiogenic)

   (B) Systemic
   - Beta Blocker
   - Corticosteroids
   - IFN α
   - Bleomycin
   - Angiogenesis Inhibitors (Future IH)

   · Topical BB

3. Surgical IH:
   - Compression
   - Sclerosing therapy
   - Embolization
   - Laser
     - Cryo
     - Radio
     - Excision

(4.) IH in specific situat

- Discussion of IH

. Cs: was the 1st line of IH. (Now BB)

. Mechanism: ?? but ± d.t.

i - VC
ii - Antiangiogenic
iii - (↑↑) Apoptosis
iv - regulate Cytokines expression

Types

- Topical (superpotent Cs)

Topical: For uncomplicated localized lesions

- Systemic

For large, deforming, Life threatening & persistent ulcerated lesions.

Funct

Topical Cs

- Topical Cs (Controversy) → Superpotent
  - Used: For periocular lesions?
- IL Cs → Effective
  - 5-40 mg/ml Triamcinolone
  - dont Exceed 3-5 mg/kg/session. (4-6w)
  - C.I: periorbital

Systemic Cs

- Indications: as before (given during proliferative phase).
- Dose: 2-3 mg/kg/d for either 2-3m. (or) until growth stops or shrinkage occurs then → Gradual withdrawal [Mean period 8m.]
- S.E:
  - GR
  - Axis suppression
  - Personality changes (irritability & sleep disruption).
  - ImmunoSuppression
  - life threatening inf.]
  - others:
    - GIT Symptoms.
    - Cushingoid
    - Neurotoxicity (d/t the preservative BenzylAlcohol) ≥ 2mg/kg For > 2ws.
    - Live-virus Vaccines

BB Better Than Cs because Rapid Relapse after Cs stop. while BB act. is Maintained.

- For large; life or function threatening lesions that resistant to systemic Cs → IFN α_{2a} or IFN α_{2b} 3 million U/m2 (daily) For 6-12m. if Failed →
  - Cyclophosphamide
  - Vincristin
  - Bleomycin
  - Propranolol
  - Embolization

Infantile Haemangioma

Epid :

[70% 1st few weeks of life (3-5 wks)
30% at birth (Cong)

(♂) > (♀) → 3 : 1

(↑ ē) ← Premature, LBW, fetal Hypoxia

- Caucasian
- soft tissue, vascular Tm of infancy.

Clp = phases

1 Nascent phase = precursor lesion — at birth

[Erythematous Macule
Telangectatic Macule ē pale Halo

rare [Bruise & scratch
ulceration → lip – perineum

---

2 proliferating phase (Max 4-6 mon) خلال أول سنة

lesion → Macule, Papule, plaque — [0.5 – 5 cm] size

site → H&N > Trunk > extremities

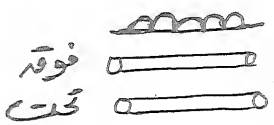
color

1 **Sup** (sup dermis, pap dermis)
- Bright red / قرمزي
- Crimson
- Strawberry lesion 50-60%

2 **deep** (deep dermis – S.C)
- blue / أزرق
- purple / موف
- Cavernous H → Warm mass 10%

3 **Mixed** → blue ē Telangectasia 30%

Hem
- Localized
- Segmental
- Multiple = disseminated



No
- Usually Single ± Multiple
  - ↓ Neonatal H

Stationary phase :- (12 - 15 mon)

No change in size

Involuting phase : (>15 mon)

Slow ↓↓ size
pale grey & ↓ firmness.

5] **Involuted phase** :-

Untt lesion → 90% → 9y; 70% → 7y; 50% → 5y; 30% → 3y

(&) → (50%) Normal skin → Sup type
(50%) Abnl skin → - Telangect, - stipple scarr, - Anetoderma, - Redundant skin, - fibro fatty reside, - Hypo pigm

No of lesions

- < 5-10 → Multiple IH
- > 5-10 → Miliary / Neonatal H
  - (+) visceral H → diffuse Neonatal H → CNS, GIT, Liver; (MR) 30-80%; ↑ Cop HF; Jeé hypothyrodism
  - (X) No visceral H → Bn Neonatal H

VB :-

A- Minimal / Arrested H = (No) proliferation phase or <25% of surface
(c/p) Reticulated erythema + Telangectesia
large ectatic vs + Some bright red- Papules

B- Cong Hem

1B Recent pathogenesis :-

Endothelial progenitor cells (EPC)
- circulate in fetus
- disappear at birth
- Jéé Remain in LBW, premature

Hypoxia of baby → ++ EPC → Haemangioma

disappearance of Epc → Regression of IH

Clo

① Ulceration : Most common (1st) ... ويجي

assē → bleeding, infection, Scarring

3 site → Lip, Neck, Anogenital

3 types → Large, Mixed, Segmental

---

② - Interfere ē function :- (5) ... وبتأثر

* periocular → Visual field dis, Amblyopia, Astigmatism, proptosis

* Lip → ulceration, feeding diff, disfigurement

* Anogenital → ulceration, Bleeding, Painful defecation, urination

* External Ear → Conductive deafness

* Nasal tip → Sup : ulcer, scar

deep, Mixed : Cartilage distortion (Cyrano Nose)

---

③ - Heart failure (HF) : ↑ Cop (dz) shift of bi to stem

- ē visceral H esp ē liver H
- ē diffuse H

NB Hepatic H ↔ HF. hypothyrodism. MRI ... اعمل

Invest

1- US

2- MRI

3- GluT-1

④ - hypothyrodism :-

dz ↑ Indothymin deIodination (in Haemangioma)

-- thyroid hormones

assē → Large cut H, Hepatic H

⑤ assē visceral H — Thyroxin level ... لازم

Syndromes ass ē IH :-

pHACES
Lyngeal
LUMBAR
PELVIC

1 P H A C E S → sternal cleft

- P → Post fossa + brain
- H → Haemangioma
- A → Angiomatosis + Arterial Anomalies
- C → Cardiac Coarctation of Aorta
- E → eye endocrine anomalies
- S → sternal cleft

---

2 L U M B A R

- L → Lower body Haemangioma
- U → Urogenital Anomalies
- M → Mylcopathy Spina bifida
- B → Bone deformity
- A → Anorectal Anomalies + Arterial Anomalies
- R → Renal Anomalies

MRI

---

3 Laryngeal – low face haemangioma :

[ass ē Cardiac Anomalies
Air way obst / RD.

ENT

---

4 Kasabach – Merrit synd :

1 - rapidly growing Vascular Tm
- → Kaposiform Haemangio endoth - elioma
- → Tufted angiomas
- → rarely cut Haemangioma

△ 2 - Thrombocytopenia ⇄ Petechae Purpura

3 - Consumption Coagulopathy.

MR 20%

ttt → Replacement therapy
Cs - Vincristine - cyclosphosphamide. Sirolimus (chemotherapy)

called = Haemangioma – Hge syndrome

NB → May occur ē Klippel synd.

---

5 P E L V I S

Synd :-
- → skin tags
- → Imperforated Anus

- P → perianal H
- E → ext genitalia Ab NL
- L → Lipo Myelo Meningocele
- V → Visceral Ab NL
- I S

Tt of IH :-

- Topical
  - IL Cs
    - Triamcinolone
  - Topical Cs
  - Imiquimode
  - Topical BB
  - Aldara
- Reassurance
  - Spont Involution
- Systemic
  - BB
  - Cs
  - INFα
  - Bleomycin
  - → Angiogenesis inhibitors
- Surgical
  - Cryo
  - Radio
  - Excision
  - Compression
  - Embolisation
  - sclerosing therapy.
- Laser

---

1. **Reassurance :-**

Nature & Involution spontaneously

2. **Medical tt :-**

- Topical
  - Uncomplicated Localized lesion
  - **Cs**
    - Mech
      - VC
      - Anti angiogenic
      - ++ Apoptosis
      - Regulate Cytokine expression
    - CI
      - Live virus Vaccine
      - Perioral !?

cs عند الأطفال وقفل بشبه

- Topical → Super potent cs
- IL Cs → 5-40 mg/mL (Triamcinolone) (or until growth stops) 8 mon
- Systemic → 2-3 mg/kg/d for (2-3 mon) (4-6 w) then (gradual Withdrawal)

SE
- Immuno suppression / GR
- life therating Infect / AXis suppression
- Personality changes, irritability, sleep disturbance
- GIT sympt
- Cushingoid
- Neurotoxicity (≥ 2mg/kg for > 2w)

(d2) preservative Benzyl Alcohol

given during proliferative phase

NB: Live virus Vaccine → (Not) before stop Cs by 1 mon.

بعد ما أوقف بشهر على الأقل

if large, life threating, Cs Resistant lesion :-

Use INF α_{2a} — INF α_{2b}

3 million U/m2 daily for 6-12 mon

if failed

- Cyclophosphamide
- Vincristin
- Bleomycin
- Propranolol
- Embolization

Mech → Antiangiogenetic

SE → Neutropenia
Fever
↑ Liver Enz
flue like sympt
irreversable Neurotoxic Spastic diplegia

BB

قبل ما تبدأ للكبير - echo

Mech → VC
VEGF ↓↓
++ apoptosis of endothelial cells

SE → 2B ↓ → Brady Cardia, Bronchospasm
2H ↓ → hypotension, hypoglycemia
Mask manif of HF

dose 2mg/kg 1 day
2-3 times bet day
6-12 mon

ē gradual Withdrawal (3 w) to avoid Rebound Tachycard

لازم يرفع كل ٣ ع ساعات وبأخذ الدوا بعدها
لازم HR < 100 اثبت الجرعة

CI → Bronchial Asthma
Cardiac dse
CNS Vascular Anomalies

* ++ ulceration Healing → Can use ē ulcerative type

inpatient	out patient
age - < 8 w	- > 8 w
- Comorbidities ← CVS CNS glucos Reg	- No Comorbidities
- Non Co-operative mum	- Cooperative mum

Laser

ND-YAG
deep & Mixed lesion

pulsed-DYe (PDL)
Sup - ulcerating - Residual

SE → ulceration
dyspigm
Scarring

↑↑ risk for SE

Surgical ttt

- involuted or partially ~ lesions
  - to Remove fibrofatty tissue & Redundant skin
- proliferating
  1. Pedunculated lesions
  2. Recalcitrant pericular lesions
  3. Recalcitrant ulcerative lesions

Cherry Angioma

Cample_De Morgan spots = Senile Angiomas

def: Most Common aquired vs proliferation.

c/p:
- Bright red
- dome-shape
- polypoidal papules

site: trunk, upper extrem

asse: aging, pregnancy, POEMS Synd.
- ↳ Glomeruloid Haemangioma

H/p: Congested ectatic Caps & post Cap Venules (papillary dermis)

IH (infantile H)	RICH (rapidly involuting Cong H)	NICH (Non involuting Cong H)
* Absent _ per-cursor _ present (at birth)	* fully developed	* Fully developed
* Rapid postNatal proliferation	* Intra uterine proliferation	* Proportionate growth
* low spont involution	* Rapid involution >1yr	* (Not) involute Spont
↑ (> girls)	(equal) but (>girls)	↑ more (> boys)
* lobular endothelial proliferation during proliferative phase * fibrofatty tissue ē involution	* Cap lobules within fibrotic Stroma containg thin walled Vs, hemosiderin.	* lobules of small, thin Wall Vs ē large Central Vs dilated, dysplastic Vs () lobules Rabnail endothelial cell.
Glut-1 Lewis-Y Ag (+Ve)	(-Ve)	(-Ve)

Kaposi Sarcoma

Is it Neoplasia ? or hyperplasia ? (21)

Low grade Mg Tm

def : Rare, Multifocal low grade Mg / Bn Tumor of vascular endothelia tissue Can affect ← Skin, m.m, L.N, Viscera ← GIT, Lung, Liver

Not Metastasis

Multifocal orgin [chem > surgery]

E :

1. onchogenic viruses :-
   - CMV
   - HPV 16
   - HHV 8 (Ks ass Herpes virus)
   - HIV

types :-

1- Classical Ks = Speradic
2- Endemic = African type
3- Epidemic = (HIV) ass Ks
4- Iatrogenic = immunosuppressive ass Ks
5- Familial

athogenesis :

This viruses Infect CD4 → Release of Angiogenetic growth factors & Cytokines → TNF, IL 1 & 6

HIV 1 transcripting Gene (Tat) → Ks ass HIV

40% → AIDs
95% → homosexual
5% → others Methods of infections

♂ : ♀ in HIV Ks = 100 : 1

Chem

			♂ : ♀
1- Classical	eastren, Western Jewish Mediterrian background	50-80 y	15 : 1
2- Endemic ← Bn nodular aggressive florid lymphadenopathy	Black afferican ← adult / child	20-40 ys / 2-15 ys	15 : 1 / 3 : 1
3- Iatrogenic → immunosuppressive	SLE transplent (Renal Recepient) lymphoma	20-60 ys, >3-30 mon after transplant	3 : 1
4- Epidemic (AIDS)	← Homosexual Men 95% / other risk group 5%	20-60 ys	100 : 1

1 Classical Ks :-

③ age → 50-80y
Sex → ♂ : ♀ 15:1
race → Europian – Eastern – Jewish

③ Skin / LN / Visceral → 10%

③ Behavior ← Course, survive, death

* Bluish-red or dark Brown-Nodules & plaques May be :-
- Hyperkeratotic / Verrucus
- Annular / serpigenous

* Affecting distal extremeties
* Acral Nodules, plaques

Visceral: GIT, Liver, Lung, Abd LN, Heart — 10%

Course = ③ Indolent, slowly progressive, Spont Resolution → pigmented scars

Death = 10% after 10ys.
- GIT Bleeding
- Ulceration
- Visceral involution

10% → Visceral / LN / death 10ys

2 Endemic Ks :-

age → 20-40 ys
Sex → M:F 15:1
race → African (black)

in children 2-15y 3:1

c/p ④

Nodular
25-40 ys
⑤ classical Ks

Aggressive = locally
large Exophytic Nodules
Fungating Tm of lower extremities locally
(−) LN → rare
(±) visceral → Sometimes
Behavior → prog ↑ in lesion & destruction of tissues & bone.
Survive → 5-8 ys

Florid = dissimenated
dissimenated Nodules
(±) LN / visceral → Sometimes / Early
Behavior → Rapid progressive, locally aggressive
→ Early visceral
→ 3-5 ys

Lymphadenopath = LN
Children
↓ Minimal skin affection
↑↑ Marked LN & visceral
Rapid progressi
Fatal ein -
→ 2-3 ys

3 Iatrogenic Ks :-

- age → 20-60y
- sex → M:F = 3:1
- race

- skin → disseminated patches, Nodules, plaques
- LN → rare ⊖
- visceral → Frequent

Behavior ↔ Indolent / Regressive ⓔ stop drug.

AE: Immunosuppression, Transplantation

---

4 Epidemic Ks :-

- Age → 20-60 ys
- Sex → M:F = 105:1
- race → HIV ptn

(STDs induced by Viral factor) — co- اثبات

- 40% of HIV → Ks
- 95% → homosexual
- 5% → hetero sexual, other

Common ē → advanced Immunosuppression → CD4 < 400

- skin → differ from Classical in:-
  - أصغر Smaller
  - أسرع Rapid progression
  - على الجانبين Bilat - Symmetrical - Extensive
  - على الخط Along line of skin cleavage ← Trunk, Face; Nose Tip → predilection site (Nose Tip)
  - أقل slight infilt ← patches, plaques, Nodules
- MM → oral (جديد) — Maybe (1st) affected site ↳ Hard palate
- LN → Frequent
- visceral → Frequent > maybe ⓔ absent skin aff.

Behavior →
- Rapid progressive
- survive 3m-5ys
- death (Not) from Ks but Infection (صفري)

Staging Classification for AIDs Related KS :-

	Good Risk (0)	Poor Risk (1)
Tumor (T)	Skin & or LN & or Minimal oral affection ↳ (Non nodular / palate) confined to	↳ oedema / ulceration. ↳ Extensive oral affection. ↳ GIT. ↳ Non Nodal Visceral affection
Immune-system (I)	CD4 ≥ 200/μL	CD4 < 200/μL
Systemic illness (S)	-Ve opportunistic infect & Thrush -Ve B Symptoms performance status ≥ 70 Karnofsky	+Ve +Ve < 70 + other HIV Related illness ↳ Neurologic

B Symptoms → [Unexplained Fever, night sweats
[> 10% involuntary wt loss, diarrhea > 2wks (persistant)

Pathology :-

Early lesion (Macules)

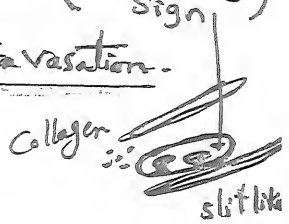
- (G.T) Granulation tissue like
- Large No of dilated caps [e] endothelial cell proliferation (protrude in the lumen)

Late Lesion (Nodules)

① - Neoplastic spindle cell proli (Spinus Vascular Spaces)

② - slit like Vascular spaces
() Collagen [e] protrusion of the newly formed Bl Vs in lumen (promontary sign)

③ RBCs extravasation.



Invest :-

① HIV ← Serology, viral load, CD4 count

② CXR = chest X-Ray

③ occult Blood in stool

④ - LFTs
- RFTs
- CBC

N.B. Visceral

Immunohistochemical stains :-

① Non specific endothelial marker * CD 34 + , CD_3 +ve

② Lymphatic endothelial Marker * D2-40 (podoplanin)

③ specific stain * Anti HHV8 Nuclear Ag

pulm invest :-

1- CXR
2- Bronchoscopy
3- CT Thallium & Gallium

Q to diff ① pulm KS infection ② intense Thallium NO Gallium

TT of KS :- Aim ← Cosmosis palliative -- progression

Limitted Ks

① lesion < 10
② No ← visceral / oral
③ Absent (-ve) Tm ass lymphoedema

Sever = Disseminated Ks

① No > 10
② (+) < visceral oral lesions
③ (+ve) lymphoedema
④ Resistant limitted Ks (~II)

- Cryotherapy
- Radiotherapy
- Alitretinoin gel
- IL - vinblastin.

Chemotherapy

IV Infussion

- Liposomal anthracyclines :-
  - PEGylated liposomal doxorubicin
  - liposomal daunorubicin
- Texanes (paclitaxel) IV infusion
- IFN-α

HIV Related :→

① HAART (±)
② IFN α (±)
③ Radiation

Texanes Anthracyclines if worsen after HAART (Immune Reconst Synd)

DD :- pseudo Kaposi ← Stasis ecz

oral lesions :-

- IL Vinblastin.
- sclerosing agent.
- Systemic therapy.

other lines of ~~tt~~ :-

- Thalidomide
- Foscarnet
- Sirolimus
- Imiquimode
- Matrix Metallo proteinase inhibitors col-3
- PDT
- Surgical

def: highly Mg Tm of vascular endothelial cells

5 types

- face & scalp
- ass ē chronic lymphoedema following radical Mastectomy
- rare death → epithilioid Angio Sarcoma (Stewart-Treves synd)
- post irradiation بعد الاشعاع

C/P

- elderly – H&N (face - scalp)
- erythermatous (or) Hge bruise like Macules and plaques
  (Cellulitis like)

Prognosis

- die ein 2-3 ys d2 Metastasis
- bad Prognosis → (12% survive for 5ys)

TT

- Surgical excision !? [Multicentric, extensive, rapidly growing, rarly successful]

---

glomus Tumor

def: Bn Tumor arising from glomus body in AV shunt called Sucquet-Horer Canal. → [Modified smooth ms cells]

Function:-

1- shut bl away from skin when exposed to cold to prevent heat loss

2- Allow Max bloodflow to skin in Hot weather to ↑ heat loss

present in dermis surr by Capsule

digit of finger-toes (esp) Subungal تحت الظفر

C/P

types: ① Solitary ② Multiple ③ Visceral

at 30-50 ys

1- small / pink / painfull / Nodule

2- Pain: Spontenous 80%, Touch 100%, Cold exposure

3- Most Common sites : fingers - Toes - penis - H & N

4- ± Nail deformity

Multiple Glomus Tm (Glomangioma)

Large , dark blue , deeper in dermis , Not painfull

± AD (Mutation in globulin Gene in ch-1)

Subtypes : 1- Localized → grouped at one area as extremetis
2- disseminated → No grouping.
3- Long plaque like

H/p :

Solitary

- Nodules Well defined
- Solid
- Endothelial lined VS spaces surrounded by clusters of
- glomus bodies & rim of Fibrous Tissue.

(Cellular) ↑ glomus cell

Glomangioma

- ill defined, less Solid Nodules!
- large endoth lined VS channels Contain (RBCs)
- Glomus Cell (Smaller) أو صغير present in Walls & arround Channels in clusters.

(Angiomatous) ↑ VS space

Clinical Tests :

① Love test : Pin or pincile tip (pressure or touch)
lool. sensitive , specific exquiste local pain

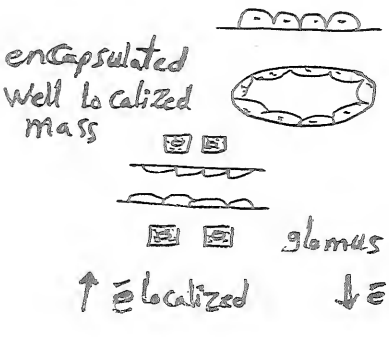
② Hibiketh test : ↓ pain induced by love test
by inducing Ischemia by tourniquet
يرفع ايده و يربط تورنيه

(-ve) No pain on touch ← تورنيه
Sever pain ← الغاء

③ Cold Immersion :

Glomus Cells

- Cuboidal
- N - Central - plump Nucleus
- C - Eosinophilic cytoplasm.



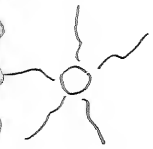
TELANGIECTASIAS

Abnormal, small, persistently dilated blood vessels visible in the skin (Fig. 106.7). Individual vessels can be discerned and range in color from light red to deep purple and will usually empty with pressure. They occur as a result of vascular dilation rather than new vessel growth and are thought to arise from capillaries, venules or small arteriovenous malformations.

CAUSES OF TELANGIECTASIAS
Primary
• Generalized essential telangiectasia • Unilateral nevoid telangiectasia • Angioma serpiginosum • Spider telangiectasias (also associated with estrogen excess) • Hereditary benign telangiectasia • Costal fringe
Secondary to physical changes or damage : Photodamage, Post radiation therapy, Traumatic, Venous hypertension
Skin disease : rosacea, PAV, involuted infantile hemangiomas
Hormonal/Metabolic : Estrogen-related (LCF, pregnancy, Exogenous estrogens) and Corticosteroids
Systemic conditions
• Carcinoid syndrome • Mastocytosis (telangiectasia macularis eruptiva perstans) • Autoimmune connective tissue diseases : SLE, DM, CREST • MF • CBCL • Angiolupoid sarcoidosis • Graft-versus-host disease (in the context of poikiloderma) • HIV infection
Congenital malformations and genodermatoses
• Cutis marmorata telangiectatica congenita • Klippel–Trenaunay syndrome • Hereditary hemorrhagic telangiectasia • Ataxia–telangiectasia • Hypotrichosis–lymphedema–telangiectasia syndrome Rombo syndrome Bloom syndrome Rothmund–Thomson syndrome Poikiloderma with neutropenia Dyskeratosis congenita XP

Telangiectasias: Disscusion

. Spider Telangiectasia: (Nevus Araneus, Spider Angioma)



- Central feeding arterial Vs (red central papule) ē radiating multiple small dilated Vs at face, Trunk & extrem.
- occurs in ① Healthy children & ♀
  ② Excess Estrogen Conditions ← pregnancy, OCPs, LCF.

Electro or Vascular laser

. Generalized Essential Telang.: Idiopathic, progressive

usually affects limbs of ♀ Adult (Trunk ±).

. unilat Nevoid:

dermatomal

- ± Cong. or Acquired (d.t excess Estrogen).
- has dermatomal distribut~ (at) Trigeminal or Cervical N.

. Angioma Serpiginosum: (DNNZ, Bolognia)

- ♀, in 1st 2 decades.
- Non-palpable, deep red to purple puncta occurs in small clusters & sheets ō may take Serpigenous outline, Annular/Gyrate or linear.
- usually unilat at Extremities (Buttocks & Legs) Evolve → Generalized (but spare: PP & MM.)

DD: Majocchi purpura (but Bilat & Biopsy)

DDx

- DD of Generalized Essential: Cut. Collagenous Vasculopathy: Central distrib. ē perivascular Type IV coll. deposit~

Hereditary Hemorrhagic Telangiect. (HHT)

(Osler_Weber Rendu d's)

- AD condition d.t Mutat^n in 2 Genes (HL)

HHT-1 → Endoglin protein

HHT-2 → ALK-1 protein

- Both Glyco-proteins are TGF-β receptors expressed on Endoth. & play role in Angiogenesis & Vs Wall integrity.

Essential. لازم

Criteria of Dx
1- Recurrent Spont. Epistaxis
2- Muco-cut Telangiect. or AVMs
3- Visceral " "
4- +ve FH of 1st degree

- Definite Dx ≥ 3 - possible: 1 or 2 (sp. early life)

- Clp → Multiple Telangiectasia ± AVM at:

1- Skin (face, Hands, Finger tips) (تتأثر بعد البلوغ)

2- Mucosal: Lips & Nose → Child ē repeated Episodes of Epistaxis (بتبدأ من الطفولة)

- Papular
- Mat like

3- GIT → Hge & Anemia.

- Hge
  - early: Nose
  - late: other organs.

4- other organs: Lung, Liver, CNS, spleen & UT.

Ataxia_Telangiectasia (Louis-Bar Synd)

(لويس بار)

- AR ; ch^ By:
  - Ataxia
  - Telangiectasia
    - Skin: Malar prominence, Eyelid, ears, popliteal & Antecubital fossae
    - Eye → linear bulbar Conjunctival Telangiect. (أول علامة تظهر عند الطفل ٢-٤ سنوات)
  - Immunodeficiency
  - Lymphomas..
  - GR
  - chromosomal instability (translocat^n bet 7 & 14 chromosomes)

3

Classification of Panniculitis (4)

Mostly Septal

- EN
- EN migrans
- Eosinophilic Panniculitis (Non-specific entity ± ass. c EN, Scleroderma, Morphea, Atypy, Lupus Panniculitis, Inf.)

Mostly Lobular

- Lupus Panniculitis
- Enzymatic (Pancreatic) Fat Necrosis
- α_1 Antitrypsin deficiency
- Sclerema Neonatorum
- S.C. Fat Necrosis of New-born
- Cytophagic Histiocytic
- Weber-Christian (Idiopathic Nodular Panniculitis, ♀, 20–40, → at LL legs → atrophic depression).
- Post-Steroid
- Traumatic
- Calciphylaxis
- Gout

Metabolic Panniculitis:
- Pancreatic
- α_1 Antitrypsin
- SCFN
- SN

With Vasculitis

DNNZ

- SVV ← small vs vasculitis
- C-PAN 2 vessel
- E. Induratum (Bazin)
- ENL
- Lucio's phenom.
- Superficial thrombophlebitis
- Rhd & Crohn's, Behçet

Mixed

- Sclerosing Panniculitis (Lipodermato-Sclerosis) CLE
- Infective
- factitious
- GA (SC), NBLD, NBXG, Scleredema
- fasciitis – Panniculitis Synd.

Erythema Nodosum

. Def- Septal panniculitis (not vasculitis), representing Hypersensitivity react- against strept. inf., TB, Sarcoidosis, IBD or it ± Idiopathic

. Etiopathogenesis: Hypersensitivity react- to stimuli:

. ﻲﻓ
1. Idiopathic (30-50%)
2. Strept Inf. (URT) (ﻖﻠﺣ، ﺰﻠﺘﻟا، ﻞﻴﺧﺪﻟا) & TB
3. Sarcoidosis (ﺎﻴﺒﻴﺼﻋ ﻲﻓ) [EN the most common Cut. Manifs of Sarcoidosis
?? Lofgren Synd: (fever, Hilar L.N, arthritis, Uveitis, HLA DRB1*03)
4. IBD & Crohn's (GIT ﻲﻓ)
5. Drugs (OCPs, Sulfa, halides)
6. Others
   - . TB: Strept ﻲﻓ ﻞﺜﻣ ﺔﻴﻠﻤﻌﻟا ﻞﻣﺎﻌﻟا ﻲﻓ ﺔﻴﻠﻤﻌﻟا developing countries ﻲﻓ ﺮﺜﻛأ
   - . Yersinia, Salmonella .. deep fungal inf.
   - . Behcet
   - . Mg (Lymphoma & leukemia ﻲﻓ ﺪﻳﺪﺷ ﺾﻔﺨﻨﻣ)
   - . pregnancy.
   - . other: viral Inf.

. Arthritis
. Constitutional Manifs → . CIP (any age but usually 18-34 ; M:F 1:4)
. EN

. flue like Symptoms FAHM. lasts 1-2ds → Erupt- (2-4 ws before erupt-)

. Arthralgia ﻞﺼﻔﻤﻟا ﻲﻓ ﻢﻟﺄﻟا → non destructive, Asymmetrical. usually → ankle, knee, wrist.

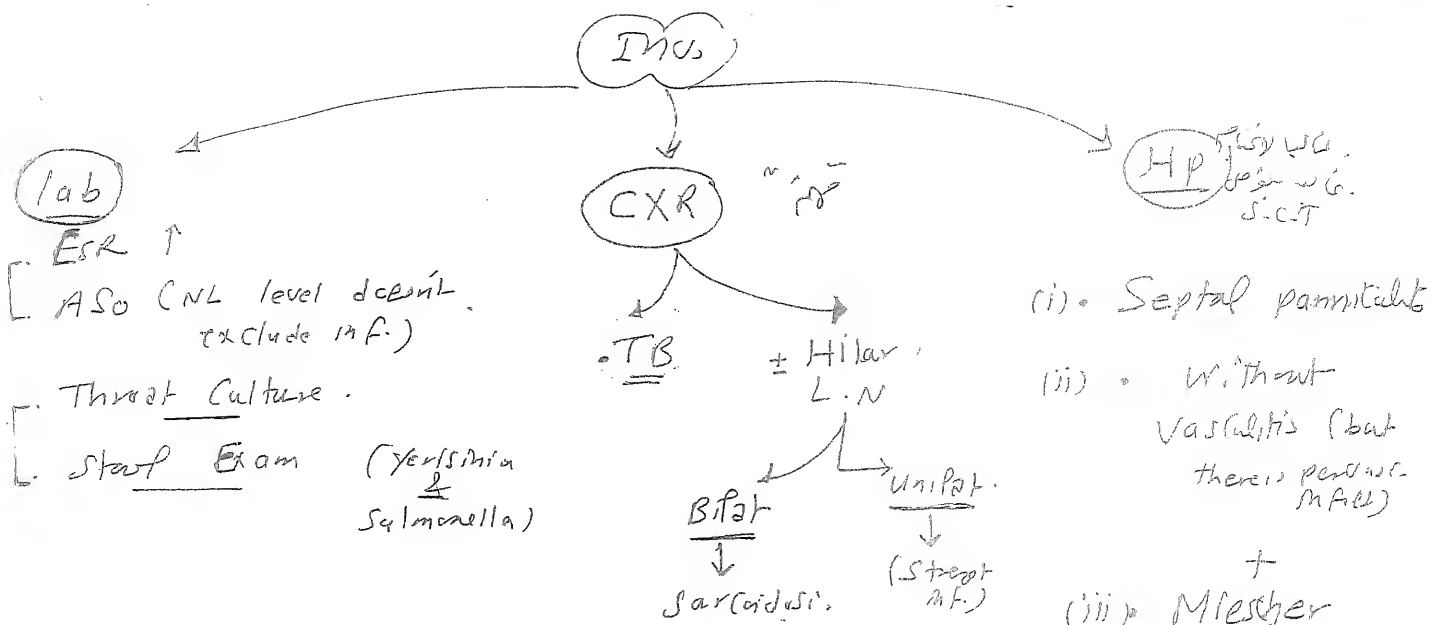
MgX : persist for ~ 6ms.

. Erupt-: Ill defined, Induration, Erythematous (Tender) Nodules & plaques at any site but prefibial area is the most common → 1w-6ms → resolut- ﻲﻓ Color changes in inf. Idiopathic (Bluish).

No Ulcerat-

. usually 3-6ws
. but ± ↓ 1w to 6m..

لا تتقيح إلا في حالة وجود عدوى بكتيرية ثانوية



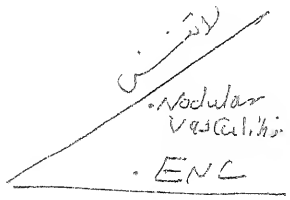
(++)

. infect. : first mixed → Granulomatous.

① Underlying Etiology:
- . Infect
- . ✱ drugs

② 1st line
- . Bed rest
- . NSAIDs
- . KI (↓ ← fever, arthralgia, Tenderness)

③ 2nd line (Severe cases)
- Cs
- Colchicine
- Dapsone
- Antimalarials.



DD of EN
(Painful Nodules at leg)

[Annals, 2012]

1. E. Nodosum (EN)
2. EN. Migrans = Sub-acute Nodular Migratory Panniculitis
3. Erythema Induratum
4. Lipodermato Sclerosis = (Sclerosing Panniculitis) — Stocking →
5. Superficial Thrombophlebitis. — Mean
6. C-PAN — Mean
7. Others — Mg (Lymphoma associated). / EN like lesions of Behcet.

DD	Details.
• EN-Migrans. (Chronic EN = Sub-acute Nodular-Migratory panniculitis) // (Villanova dis) ♀ 30-60 (E. med.)	• Single Nodule / plaque: . Unilat. . painless. • Enalages: peripheral extension ē Centrap Healing ē yellow hue or Morpheaform Centre. . Migrate: after wks - mo.

H: ILC . KI (or) Systemic Cs

DD.

Sclerosing panniculitis
Lipodermatosclerosis

- Etiopath
  1. Venous stasis
  2. " insufficiency & HTN
  3. Coagulopathy
- CLP (Uni or Bilat.)
  - Acute stage: Indurated, Erythematous, Tender, Hot, plaques at inner leg above the ankle. (Cellulitis like)
  - Chr. stage (Chr-Y): [Sclerosis] ↓ Pain, Induration, redness, Hyperpigm. + VV ± leg ulcers.

(Stocking distrib = Inverted Champagne Bottle = Bowling pin.

- HP → Mixed panniculitis

- US & MRI → to define Extent of dis. & possibility of Vascular surgery.

- (tt) Elastic Compression therapy لازم
  Venous Stasis علاج
  1. Vein surgery (laser ablate or sclerotherapy)
  2. ↓ w.l. 3. US tt → ↓ fibrosis.
  4. fibrinolytic: Streptokinase
  5. Trental: ↑ Flow & Blood.
  6. Topical Cs: ↓ inflamm (early)
  7. Horse chestnut extract: ✓ in venous dis

Superficial Thrombophlebitis
Behcet

- Et → 1. Coagulopathy. (as lipoderm. also)
  2. Venous insufficiency, DVT & VV
  3. Traumatic: IV lines infect

Superficial thrombophlebitis

- C/P : Linear (along path of vein) ; Multiple, Tender Nodules usually at Lower legs (great saphenous vein).

Tx: Conservative
- leg elevation, Compression Stocking.
- NSAIDs, Antibiotics.
- LMWH

Surgical
- Puncture & Evacuation → of affected vein
- Surgical Excision of affected vein.

Polyarteritis Nodosa (PAN)
(Periarteritis Nodosa)

- Def. Segmental, Necrotizing, Medium Sized Vasculitis affecting Medium Sized aa commonly at their branching points (Coronary, Hepatic, renal, Cut.) → aneurysm or Stenosis

- Types:
  - Systemic: d.t HBV
  - Cut.: d.t Strept. or Drugs.
  - others: FMF, SLE, IBD, Drugs.

- C/P:
  - Systemic (90%): Systemic affection of aa of (renal, Coronary, Hepatic, CNS)
  - Cut. (10%): → Chr. relapsing Course:
    - Painful S.C. Nodules along Course of BVs mostly Legs
    - Cut. ulcers
    - Livedo Reticularis.

Burst pattern of Livedo around leg ulcers → CPAN

- HP
- LCV of (Small, Medium sized BVs) ± Septal panniculitis.

* Treatment
- Etiolgy → Stop Drugs, ↑↑ of HBV (IFNα + Vidarabin).
- Cut.: NSAIDs, Cs (Topical & Systemic), Colchicine
  Systemic: Systemic Cs & other Immunosuppressive (Dapsone).

Others

1. Lymphomas:
   - CTCL
   - CBCL

2 Types of TCL:
1. S.C. panniculitis like TCL (SPTL)
2. Nasal Type NK/TCL (Nasal NKT)

↓

Both show S.C Nodules at leg & ± Trunk ± B Symptoms (Fever, Fatigue & W.↓ loss)

HP diff.:
- SPLT: riming of fat cells by Mg Tcells.
- NK/TCL: Angiocentricity + agngio destruct + Necrosis.

Immunophenotyping
- SPLT: CD4+, EBV−
- NK/TCL: CD56, EBV+ve

Indolent Course ↑ SPLT

Aggressive ↑ NK/TCL

② EN-like lesions of Behcet-

- to diff. from Classical lesions:
  - (A) Clinically: at trunk, UL & buttocks.
  - (B) HP: Lobular or Mixed Panniculitis + Vasculitis

DD of Palmo-plantar Painful Nodules in Children (Painful-Plantar Erythema)

1. palmo-plantar EN
2. Acute traumatic urticaria (HP) (No s.c.t affected)
3. Pseudomonas-Hot-feet Synd.
4. Recurrent PP Hidradenitis (Plantar Panniculitis)
   - HP: Neut. infilt. in Coils of Eccrine & dermis.
5. Cold panniculitis.

delayed-pressure ppt by physical Trauma

• α_1 - Antitrypsin deficiency panniculitis:

. Glycoprotein. produced by liver

. (F) [1] Tissue degradat^{-}
[2] Immuno Suppressive → ↓ inflammat^{-}.

. Cause of deficiency : Genetic.

Lower back buttocks Thighs

. C/P : large, Erythematous - Purpuric, Tender Nodules & plaques at lower Trunk & proximal extremities

→ Severe Necrosis & Ulcerat^{-} ē oily discharge.

. others fever, Emphysema, Pulm. Embol., Angioedema

. Inv. . (Lab) α_1 Antitrypsin level. (< 5 mg/dl)

. (HP) Panniculitis ch BY (dermal & S.C.T)

. Severe liquefactive Necrosis → Separat^{-} of lobules from Septae.

. Hge, ± Vasculits.

. infil. early Neut. later Lymphocytes ē Histiocytes

. Tt → No effective Tt

(1) Tx → IV infusion of α_1 antitrypsin.
6 mg/Kg/w → rapid Improvement

(2) Others: . Cs
. Dapsone
. Colchicine
. Doxy.

- **Cold panniculitis**
  - d.t exposure to cold
  - S.C Erythem. – Blush. Nodules
  - Self limiting

- **Factitial P.**
  - Self inflicted by [Blunt Trauma / or inject= of drugs (Morphine, Pentazocin)]
  - Chr., ulcerative, at thigh ass. ē Woody. indurat=.

- **Traumatic P.** (4 Types of injury)
  - Cold panniculitis
  - Sclerosing – Lipogranuloma
  - Infectable ✗
  - Blunt. Trauma.
  - Post irradiat= or radiat= recall dermatitis.

Geometric ulcerat=

- **Infective Panniculitis:**
  - occurs in Immuno-Compromised
  - Etiology
    1. Bact. ← G+ve / G-ve / Mycobact. (كل واحد)
    2. Viral: CMV
    3. Fungal: S.C & Systemic Types.
  - HP: Neutrophilic lobular Panniculitis (± Septal)

- **Post-Steroid**
  - يتحول لأطفال
  - لو حصل توقف
  - ضامن للكل يكرش

- **Lipoatrophic**
  - Autoimmune Type ass. ē Autoimmune dis (AICTD, R.A, DM) ⟶ Head ē Lipoatrophy.

- **Pancreatic P.:** (Enzymatic)
  - Pt. ē Pancreatic dis < Pancreatitis / Carcinoma
  - ⟶ Enzymes (Amylase, lipases, Trypsin)
  - ⟶ lobular Necrosis of S.C.T
  - Clin: Systemic: fever, arthritis, abd. pain, Eosinophilia & pleural Effusion. (Visceral fat involvement)
  - (2) Cut. S.C. Nodules (Tender or Asympt.) 1-3 ms Resolut= or ulcerat=: exude ⟶ Thick brown oily Material (Liquefactive Necrosis).

- Inv.: Serum
  - Lab: ↑ Amylase & lipases.
- HP: ① Basophilic Necrosis (in Lupus P. → Eos. hyaline-Necrosis).
  - Lost-Nuclei + Shadowy Thick walls → ② Ghost lipocytes:
  - ③ Saponificat=: Ca + fat (Basophilic material)
- Dd: underlying Pancreatic problem (أي سبب)
  - لازم يكون عندك Pancreatic dis.
  - لازم يكون عندك Pancreatic dis.

Panniculitides with needle-shaped clefts in the subcutis.

Condition	Type of patient	C/P	Complications	Histopathology
Sclerema neonatorum (SN)	-Severely ill premature neonates - 1st week -Ppt by: hypothermia (also, asphyxia dehydration, defective complement)	- Cool, waxy, rigid and board-like skin - Bad prognosis	- RD - CHF - Diarrhoea - Death from septicemia, in three-fourths of cases	- Thickened fibrous septae - Minimal inflammation and infilteration - Needle-shaped clefts in lipocytes ONLY
Subcutaneous fat necrosis of the newborn (SCFN) (Adiponecrosis subcutanea)	-Full-term healthy - 2-3 Ws -Ppt by: Hypothermia (also,hypoglycemia due to gestational DM, meconium aspiration, preeclampsia)	- Discrete SC, firm movable nodules and plaques - Excellent prognosis, self-limiting	-Hypercalcemia (onset may be delayed for several months, Causes seizures and nephrocalcinosis), -Thrombocytopenia, -Hypertriglyceridemia	-Lobular panniculitis -Marked inflammation with granulomatous infilteration - needle- shaped clefts (crystals) within lipocytes and giant cells; -/+ calcification and Hge
Poststeroid panniculitis	-Children (1–14 ys) - Ppt by: rapid withdrawal of corticosteroids (after 1-40ds).	As SCFN	Underlying conditions treated with systemic corticosteroids have included leukemia, cerebral edema, nephrotic syndrome, secretory diarrhea, acute rheumatic fever	As SCFN (but no calcification and Hge)

NB: There are three entities--sclerema neonatorum, subcutaneous fat necrosis of the newborn, and poststeroid panniculitis--that are characterized histologically by formation of needle-shaped clefts within lipocytes. In contrast to adult fat, the subcutaneous fat of infants is thought to be prone to crystal formation because of a higher content of saturated fatty acids, including palmitic and stearic acids, and a relatively lower content of unsaturated fatty acids, such as oleic acid[68]. This increased saturated to unsaturated fatty acid ratio results in a higher melting point for stored fat and promotes crystallization under certain conditions. Microsized crystals (type A) apparently do not produce an inflammatory response; they are actually common (in a widely dispersed form) in healthy infants 6 months of age or less, but are more numerous in sclerema neonatorum. Larger, type B crystals that tend to be arranged in rosettes are capable of eliciting a granulomatous response; these crystal types are most often seen in subcutaneous fat necrosis of the newborn and poststeroid panniculitis[68,69]. Crystallization and defects in fat mobilization account for the clinical findings in these disorders.

Phagocytose other Cells ↓

Cytophagic Histiocytic Panniculitis.

(. Panniculitis)
(. Erythema.)

- Panniculitis ch BY infil. by Histiocytes & other inflamm. cells → fat breakdown & Hge
  Engulfing of other cells (WBCs (++) RBCs) By Histiocytes.

- Cp ① Systemic
  - Fever
  - HSM — LCF / Jaundice
  - Pancytopenia (inf. organ infil. by phagocytes).
  - Hge (GIT, Renal, RT)

  ② Cut. → Panniculitis.

- Etiology
  - Bg
  - Mg
  - Inf. (HSV)
  - Immune Suppression
  - S.C TCL

- HP : . lobular (or Mixed) Panniculitis
  . Infil.
  - Lymphocytes (+++)
  - Macrophages — Typical / Enlarged
  - other cells

  Cytophagia

  Engulf. RBC, WBCs, karyorrhectic debris [Bean-Bag Cells]

. NB in Cases of SC TCL → the typical cells do Immunophenotyping or TCR Gene analysis

- Tt
  - Cs
  - Cicosporin
  - Dapsone
  - Chemotherapy. (CHOP)
  - IVIG.

. Cold Panniculitis

↓

. Type of Cold injury to S.C.T

Etiopathogenesis (Types of patient):

1. Newborn, Infants & children

↓ higher Saturated : unsaturated Fatty acids

→ higher melting & solidifrate points of Stored fat. → (4 Patterns)

(i). Ice therapy : 1st line tt of SV. Tachycardia

(ii). SN

(iii). SCFN of Newborn ← Today

(iv). children → Popsicle Panniculitis (< Cheeks / Chin)

2. Obese ♀ exposed to Cold → thighs, buttocks & abdomen / arms, Chin.

3. Equestrian Panniculitis : exposure to Cold during Wearing tight fitting Clothes.

4. Patients ē < Perniosis & Paralyzed limbs

CIP : . Cold exposure 2ds → < ± Systemic illness

Cut. lesions : firm. Hard, Erytham. Violaceous, illdefined, Cold, Painful. plaques & Nodules.

. Children : Popsicle Panniculitis at ..

. obese ♀ ??

. Paralyzed limb or limbs having Perniosis.

→ SN & SCFN ← Site

See below

HP

Lobular (± Septal) Panniculitis.

Mucin deposits (ōg) [No Needle Clefts except in <]

Patchy lymphohistiocytic infilt. ē Eos.

TTT

. most Self limiting

. rewarming

. Systemic ⅓

. Topical ⅔